# THE American Journal OF Gastroenterology

VOL. 27, NO. 4 APRIL, 1957

Panel Discussion on Esophageal Varices
–Portal Hypertension

Selection of Operation for Gastric Ulcer

The Urinary Lipase Test as an Aid in the Diagnosis of Carcinoma of the Pancreas

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***Twenty-second Annual Convention***
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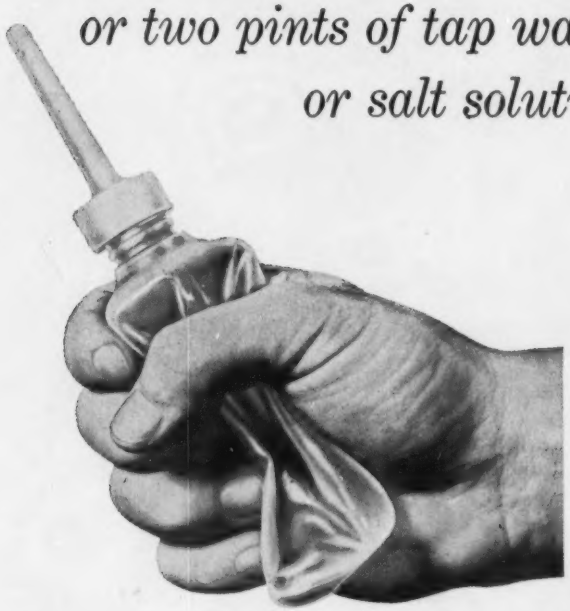

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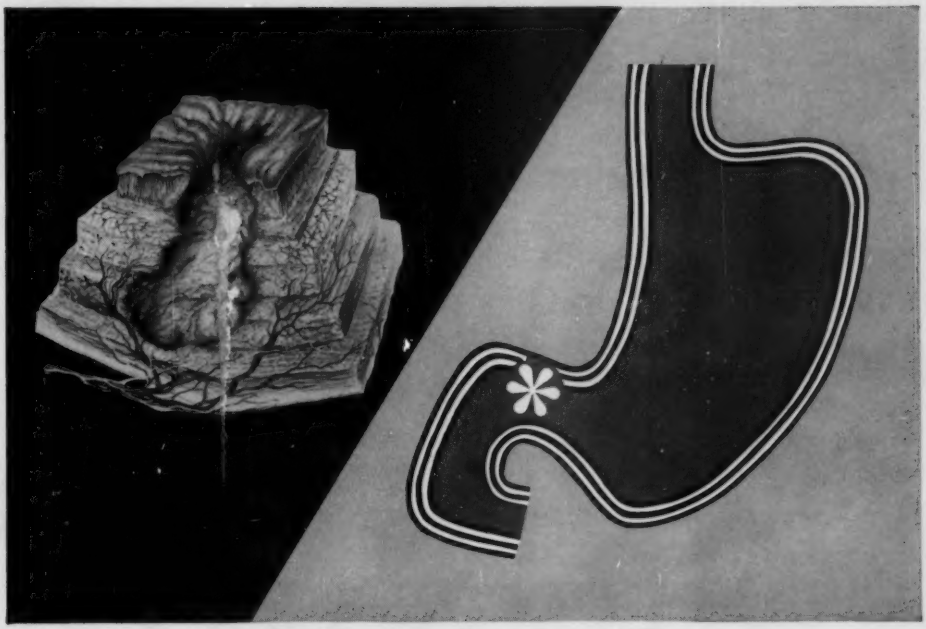

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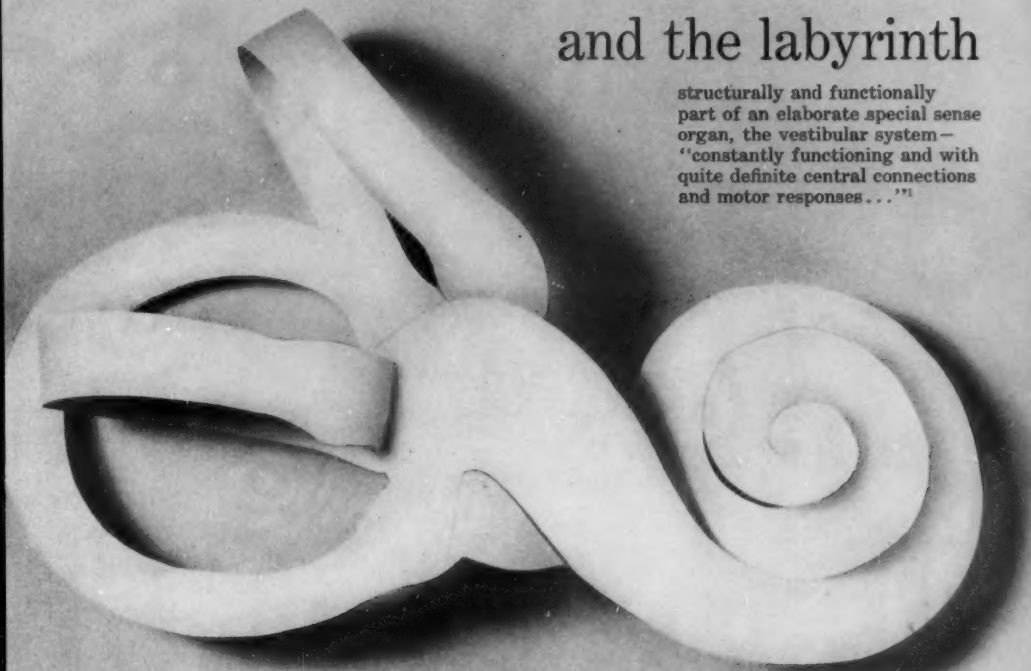

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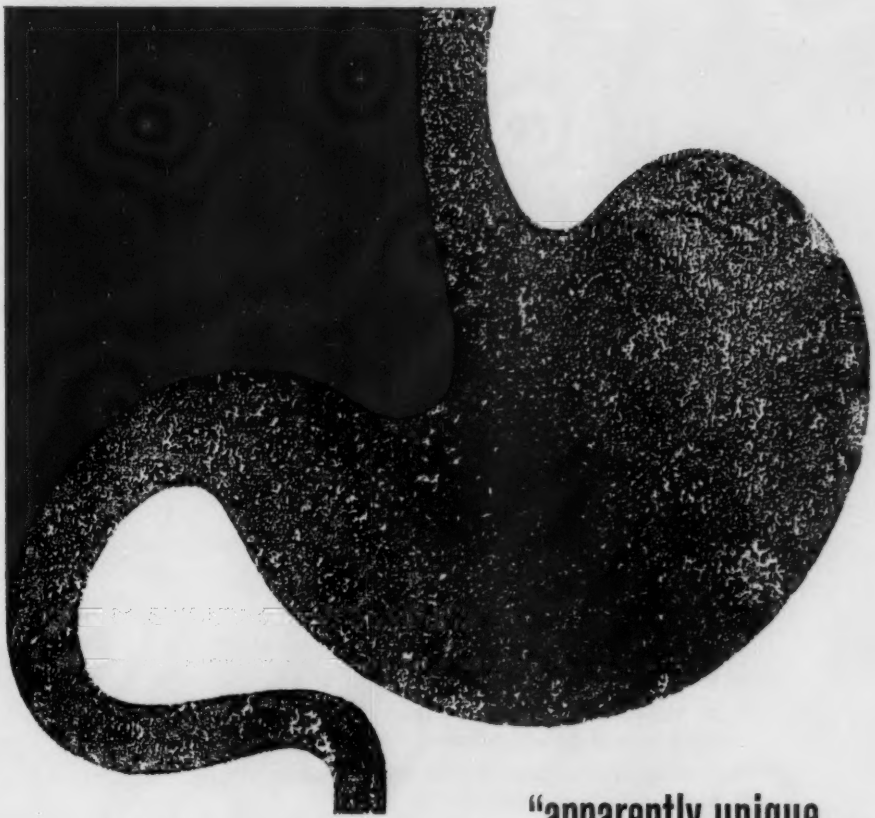

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VOLUME 27 APRIL, 1957 NUMBER 4

# PANEL DISCUSSION ON ESOPHAGEAL VARICES—PORTAL HYPERTENSION*

HIRSCH R. LIEBOWITZ, M.D., Moderator†

FRANCIS F. RUZICKA, JR., A.B., M.D.‡

LOUIS M. ROUSSELOT, A.B., M.D., M.S. (Surg.), Med. Sc.D. (Surg.)¶

New York, N. Y.

and

CARL H. GREENE, A.B., M.D.§

Brooklyn, N. Y.

*Dr. Hirsch R. Liebowitz:*—Participating members of the panel are Dr. Francis F. Ruzicka, Jr.; Clinical Professor of Radiology and Director of Radiology, St. Vincent's Hospital; Dr. Louis M. Rousselot, Professor of Clinical Surgery and Director of Surgery, St. Vincent's Hospital; and Dr. Carl H. Greene, Associate Professor of Clinical Medicine and Visiting Physician at Bellevue Hospital.

I think we may profitably initiate the discussion by mentioning the various modalities that are employed to establish a diagnosis of portal hypertension. Clinically, the presence of a dilated superficial collateral circulation and enlarged spleen, and hypersplenism are convincing criteria, but these may nevertheless be absent. Endoscopy is a valuable procedure in establishing the presence of varices. The diagnosis is conclusively made by actual measurement of the portal pressure. This may be performed by direct puncture of the varix itself through an esophagoscope, from a large collateral abdominal vein, or by occlusive hepatic vein catheterization. Another practical method consists in assay of the intrasplenic pulp pressure, which also reflects the tension existing

*Presented before the Third Annual Convention of the American College of Gastroenterology, New York, N. Y., 15, 16, 17 October 1956.

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in the portal circuit. The most convenient approach, however, is to visualize the varicosities by x-ray examination and Dr. Ruzicka will make some comments on this phase of the diagnosis.

*Dr. Francis F. Ruzicka, Jr.*:—The roentgen methods of examination for determination of esophageal varices and a study of portal hypertension are two:

1. The barium swallow, with which we are all familiar, used for demonstration of varices in the esophagus; attempt also is made to visualize varices in the cardia of the stomach.

2. The portal venogram. We shall delay discussion of this method for the purpose of division of material.

The demonstration of varices by barium swallow is not only indicative of the presence of such varices, but also suggests the presence of portal hypertension. Templeton states in his textbook (1944) that in a study using postmortem material, the esophagram showed varices in approximately 40 per cent of the cases that actually had varices. I think this is a rather low figure. There are higher figures than this.

Atkinson and a group of British workers in London*, have more recently found that the esophagram, in their experience, demonstrated varices in about 60 per cent of individuals in whom varices were shown by portal venography. They state that in no case were varices revealed by another method where portal venography had failed to reveal them. Endoscopy in the same series showed varices in 83 per cent of the cases.

There are varices which may be seen only by endoscopy, and varices which may be seen only by the esophagram. It is important to realize that the two examinations can often be supplementary to one another and where one may fail, the other may be successful. I cannot tell you when this will occur, but in the event of a failure, it is certainly indicated that we go on to the use of the other method.

Dr. John Evans of New York Hospital, in a personal communication, has stated that in an evaluation of the accuracy of the esophagram as a method of study, varices were demonstrated in 75 to 80 per cent of cases. These cases were verified by venography, by postmortem material, and endoscopy. Dr. Evans attributes this high figure to the meticulous care in the examination. Obviously carefulness and expertness in examination will influence the end-results.

In the examination of the esophagus, a barium paste is employed. It is well to use a relatively thin paste and yet too thin a paste or too thick a paste may not coat the esophagus adequately. The paste should be of such consistency

*The Clinical Investigation of the Portal Circulation with Special Reference to Portal Venography—Quart. J. Med., **24**:93 (Jan.), 1955.

that it is like melted ice cream which will just about pour off the edge of a spoon if the spoon is tilted about 45 degrees. In this way one avoids the situation where the barium is too thin and in passing does not coat the esophagus, or where a large heavy bolus, passing through the esophagus, will compress the esophageal veins so that they will not be visible on the roentgenogram. Of greatest importance in the examination is the careful making of spot films which permits filming at the optimum moment. These are made in various positions, on inspiration, with and without the Valsalva maneuver. Some authors recommend the use of the Mueller maneuver to bring out the varices. Following this, large 14 x 17 routine films are obtained in the usual way. The right anterior oblique and right lateral positions are perhaps the most advantageous.

The barium method is quite unsatisfactory for demonstrating varices in the cardia of the stomach because the normal rugal pattern may simulate varices. A large group of varices may appear as an intramural or mucosal filling-defect in the cardia, even simulating carcinoma. The portal venogram here plays a very much more satisfactory role in demonstrating varices.

Another useful application of the esophagram is in the follow-up of patients who have had portacaval surgery. In a recent personal communication Dr. Evans stated that in his study the cases who had portacaval surgery showed a tendency for the varices to disappear. In those in whom the shunt had closed with thrombus, however, the varices again appeared prominent. We have observed this same phenomenon. Perhaps Dr. Rousselot will refer to this later in the discussion.

*Dr. Liebowitz:*—Dr. Evans' experience at the New York Hospital indicates a high incidence of gastric varices by the radiologic technic. In 40 cases of portal hypertension, he was able to demonstrate 20 definite and five very suspicious cases of gastric varices. Are gastric varices, in your experience, demonstrable in such appreciable incidence in association with esophageal varices?

*Dr. Ruzicka:*—We have made the attempt, but because of the confusion with the gastric mucous membrane pattern, we have frequently been unable to be certain of varices. When they are very large and prominent, then one can feel fairly certain, but when they are smaller it is more difficult.

*Dr. Liebowitz:*—The precise manner in which varices rupture is a controversial subject. Clarification of this question is important because upon its solution depends the application of sound medical and surgical principles of treatment of the resulting hemorrhage, and also the institution of prophylactic measures that might postpone or prevent this catastrophe.

Two causes have been advanced to account for varix rupture—an increased hydrostatic pressure and erosion of the varix secondary to a reflux esophagitis. Essentially the question may be posed: Is rupture erosive from without or eruptive from within? I have been particularly interested in this phase of the

varix problem. In a survey of a large series of cases of varix rupture at Bellevue Hospital, it was found that bouts of coughing, retching and vomiting, passage of a Levin tube, ingestion of a large meal, acts of physical violence, administration of intravenous albumin and ACTH preceded and seemed to precipitate varix rupture and bleeding. These physiologic acts have both direct and indirect influence on the magnitude and dimension of the varices, and hence on their integrity, by effecting changes in portal and splanchnic blood flow and portal pressure. Let us, for example, examine the alterations that are prompted by coughing or vomiting. The negative thoracic pressure has a dilating effect on the varices. During the phase of inspiration, the varices enlarge and this may be objectively confirmed through the esophagoscope. The suction action within the chest resulting from respiratory movements of the thoracic cage plus the intraabdominal pressure, are concerned with the transfer of blood heartward from the splanchnic basin into the chest. During a spasm of coughing or vomiting, the portal pressure rises precipitously, and the heightened portal pressure gradient is transferred through the cardioesophageal collateral pathways into the varices themselves. This may be measured through a needle resting directly in the varices through an indwelling portal vein catheter or by the method of hepatic vein wedging. The net result of such physiologic acts is a sudden engorgement of the delicate and thin-walled varices and peak rises in intravariceal pressure that results in their rupture.

Following the ingestion of food, the vigorous contractions of the stomach musculature, as part of the digestive process, prompts more blood flow and at a greater rate into the coronary vein which communicates with the esophageal plexus. During periods of physical violence (fall out of bed, epileptiform seizures, agitated states, blow on the abdomen) entailing sudden abdominal wall contraction and exaggerated respiratory movements, fixation of the diaphragm and increased intrathoracic and intraabdominal pressure, hemodynamic changes transpire that promote rupture and bleeding.

Many students of the disorder of portal hypertension subscribe to the concept that an antecedent inflammation of the esophageal mucosa is an important prerequisite to rupture from varices; and that direct communication between the varicose vein and the esophageal lumen is achieved through erosion of the vessel wall by an ulcerative esophagitis with resultant hemorrhage. The exponents of this view consider the pathogenesis of the esophagitis to be due to regurgitation of acid peptic juice from the stomach. This concept is based on the studies of Wangensteen, and the demonstration of an appreciable incidence of esophagitis in cases of varices that have gone on to rupture.

Peptic esophagitis, however, is encountered in patients with achlorhydria, following total gastrectomy and as a sequel of surgical procedures on the stomach specifically designed to curtail gastric secretory activity. Thus the causative role of pepsin and gastric acidity in its production may be questioned.

Its presence in patients that simultaneously rupture from varices may rather predominantly be due to preagonal changes, or a product of stress. Shock occasioned by pronounced hemorrhage cannot be surpassed as an exemplary form of stress. Too, the morbid changes in the lower esophagus may also, in part, be due to the dynamic circulatory changes that accompany varicose dilatation. Venous congestion and stagnation induce an avascular epithelium that leads to nutritional impairment of the mucosa with consequent edema, degenerative changes and ulceration.

It is my conviction that rupture primarily is due to an increased hydrostatic pressure. As a result of the augmented internal dynamic force, the veins become overdistended and thin-walled and assume a more peripheral position separated from the esophageal lumen only by the epithelium which normally is 0.2 mm. thick. In the advanced stage, the mucosa may disappear over the largest varicose dilatations whose walls actually come to form part of the lining of the esophagus. This anatomical and vascular transformation, wrought by the expanding force of the high portal pressure, is but one step removed from actual bursting of the vein wall. A sudden paroxysmal rise in the portal hypertension by such acts as coughing, retching, vomiting, etc., is sufficient to provide the final assault and cause a mechanical breach in the varix wall barrier. Rupture on the basis of an expanding blood volume and distended portal bed, produced by intravenous albumin or ACTH bespeaks a similar mechanism. When at autopsy one sees varicose veins that have been torn wide open for their whole length, it is only conceivable that an internal eruptive force could have been responsible for initiating such havoc. The best proof that a primary peptic acid esophagitis is not the essential mechanism is evident in the fact that cecal, jejunal, diaphragmatic and sigmoid varices are also the site of rupture and hemorrhage. Varices both in the esophagus and jejunum have also ruptured following a total gastrectomy. An acid peptic erosive mechanism cannot, of course, be implicated in the rupture in the aforestated circumstances.

Following this aspect of the discussion, we should like to take up the subject of control of varix bleeding. In New York, Blakemore perseveres in balloon tamponade compression of the leaking varix; in Boston, Linton subscribes to prompt transesophageal suturing of the varicosities; in Philadelphia, O'Sullivan has engaged in emergency portacaval shunts to arrest the hemorrhage; in other areas, some individuals are doing an emergency esophagogastrectomy. Dr. Rousselot, will you give us an expression of your opinion about these various therapeutic modalities?

*Dr. Louis M. Rousselot:*–Yes, Dr. Liebowitz.

In this area of emergency therapy of portal hypertension and the bleeding varix, I think it is important to begin our remarks with a reiteration of the lethal aspects of bleeding from this particular lesion. Unlike bleeding from peptic ulcer, which forms the great majority of upper gastrointestinal bleeding, in our

clinical experience, the frequency of bleeding varix certainly has been rising materially within recent years, and some clinics report an incidence of 15 per cent of their cases are bleeding varices.

Unlike the bleeding peptic ulcer, in which instance we have a cushion, if you will, the initial bleeding from the varix in portal hypertension may be so massive and so severe as to be the fatal bleeding episode. In a number of series of studies of the life cycle of cirrhosis, and with particular reference to the bleeding varix, and also in an analysis of our own cases over the past five years, there has been a fatal issue in approximately 33 per cent of these cases with the first hemorrhage. It is obvious that we are dealing with something that has considerable punch.

The emergency treatment using the balloon tamponade in these cases, I might say, represents its use in one of the few areas where there is fairly good agreement. Most of the clinics throughout the country are utilizing some form of balloon tamponade, the Blakemore double balloon type, or the Nacheles single balloon tube with multiple lumina.

I might digress just for a moment to mention that I feel personally that the balloon tamponade is also useful as a diagnostic tool in addition to its value as a therapeutic maneuver. In the unknown case of bleeding, that case which we all so frequently encounter, without any previous history; with no story of a chronic peptic ulcer; nothing that suggests cirrhosis, or any other lesion such as gastric neoplasm, when we are faced with an initial episode of serious massive bleeding, passage of a tube can be distinctly helpful.

If hemorrhage is promptly arrested, the presumption is very strong that we are dealing with a varix. If hemorrhage is not promptly arrested, we have two possibilities: that we are dealing with a bleeding varix in a gastric varix bed, or some other lesion of the upper intestinal tract.

We have utilized the gastroesophageal tamponade and, as Dr. Liebowitz stated, it is not absolute, but it is distinctly helpful in controlling the bleeding in some two-thirds of the cases. We institute it immediately when the gastrointestinal series has been completed, and I think Dr. Ruzicka did not emphasize the fact that we routinely carry out emergency gastrointestinal series in all our unknowns, and feel that it is of distinct help. It does, however, let us down on occasion, and the balloon tamponade routine follows, with supportive therapy, including transfusion, administration of Vitamin K. In those instances where we feel that we are dealing with varices, with an arrest of hemorrhage, we will then also proceed with the institution of intestinal antibiotics and intestinal purging to empty the bowel of old blood, with the deleterious effects that it may have in an alteration of ammonia metabolism.

I think Dr. Greene will speak further on that, so I will not intrude on his domain.

Now, if we are faced with a situation in which bleeding continues after balloon tamponade, we feel that early surgery is indicated, and our own plan of attack is to approach the gastric pouch from below, from the transabdominal route. Our reason for doing that is we still feel that the bleeding site has not been demonstrated, and by an abdominal approach, a gastric exposition of the stomach can be carried out. The stomach and the duodenum can be seen, and explored.

In the fortunate situation we may immediately find either gastric ulcer or gastric neoplasm, or we might find duodenal ulcer, or we might find both. Duodenal and gastric ulcer together do not represent a rare situation. Finally, we may feel nothing other than a sac full of blood, and in such a situation, it is most important that the gastric pouch is opened through a gastrotomy wound; the interior of the stomach is carefully and gently irrigated with saline and not with the rough introduction of pads, which of themselves may initiate superficial erosion and hemorrhage, and color the picture for the operator, but with careful exploration of the interior of the stomach and duodenum.

The next bit of information that the surgeon can obtain is that he can demonstrate whether the bleeding is coming distally from beyond the pylorus, whether it is coming from the gastric mucosa in terms of erosion, or superficial ulceration, superficial gastritis, or, finally, whether it is coming from the gastric cardia from a varix.

If, of course, we are dealing with an ulcer, the orthodox management, that is, subtotal resection of the stomach, is carried out. If bleeding varix is found, and if the bleeding is from the gastric side, we believe that the technic of Welch, is extremely valuable. That is the over-sewing of the bleeding point.

Now, this may not be successful, in which case the incision must be extended, the abdominal incision, to the thorax, the gastric wound then closed, and a radical procedure instituted, to wit, an esophagogastrectomy. The latter procedure is an extremely formidable one, and one that carries with it, in our hands, a mortality in the neighborhood of 40 to 50 per cent.

Our experience has been small, because we have carried this out only as an heroic gesture, in five cases. We feel that tamponade will be successful in most cases, thus precluding emergency surgery.

Now, in the situation in which tamponade therapy is successful, and the presumption is that we have bleeding from the esophageal side, the next sequence of events may be detailed as follows, and here there is extreme controversy, again: Dr. Liebowitz mentioned the philosophy of carrying on prolonged tamponade, upwards of a week or more. I spoke to Dr. Linton only last week, and he has modified his initial 24- to 48-hour waiting period. He claims that he is now shortening it to a period of 12 hours, when he first begins to decompress

to see whether he gets bleeding from the esophageal side and then makes his decision concerning emergency surgery.

So, you see the direction of thought. Our own practice in the past has been to carry on a tamponade for a period of 24 hours, and in 24 to 48 hours again, decompress and see whether bleeding recurs. If bleeding recurs in that time, we agree with most other workers in this field, that prolonged alternation of tamponade and decompression, tamponade and decompression, is extremely undesirable; that repeated hemorrhage is a major factor in increasing hepatic anoxia, and further induction of hepatic failure of the type that comes from ammonia intoxication.

Our feeling is that if the patient seems to be a very good, or fairly good risk, that type of patient should have surgery and, if he is an extremely good risk, then we feel that esophagogastrectomy or emergency portacaval shunt is preferable to ligation.

Linton somewhat ridicules the idea of esophagogastrectomy, stating that he feels it is pretty much the same as doing an abdominoperineal resection for hemorrhoids. That is a very facetious position to take. Certainly bleeding esophageal varices present a threat that hemorrhoids never present. It is the problem of sending a man after a man's job and not sending a boy.

One other approach to this problem of emergency surgery has been proposed, and Dr. Liebowitz mentioned it briefly; that is the carrying out of an emergency portacaval shunt. O'Sullivan has reported carrying it out in 9 cases, and they were all very severe, massive bleeders. Two of his cases were distinctly poor risk cases, and in spite of that he was able to get through with a 33 per cent mortality.

I have distinctly an open mind on this latter situation. It may prove to be more effective than the other methods mentioned. Our own hesitancy in utilizing this as an emergency surgical procedure has been the fact that these are depleted patients, usually with low serum protein, usually with considerable tissue edema. We hesitate to carry out the vascular anastomosis with tissues in that category, feeling that we may be facing a very prompt and early thrombosis. That is the picture as of today.

To briefly review, again, there are four types of emergency surgery for bleeding varices. One is transesophageal ligation, as advocated by Linton; one is the transabdominal gastroesophageal ligation as advocated by Stuart Welch; one is esophagogastrectomy, as advocated by a number of individuals, including ourselves, but we again state that we are definitely on the fence; and, finally, emergency portacaval shunt, as advocated by O'Sullivan.

I think, Dr. Liebowitz, I will call a halt at this point because we still have a good deal to cover, and I know you have several definite ideas in mind.

*Dr. Liebowitz:*—Since Dr. Rousselot mentioned that his initial approach is through the abdomen to make sure that there are no other causative lesions, it is wise to emphasize that in about 20 per cent of portal hypertensive cases and associated definite established varices, a cause other than varicosities is responsible for the hemorrhage. It has been shown that the incidence of peptic ulcer is higher in cirrhotics than in the general population. We recently posted several cases of cirrhosis with unruptured esophageal varices who bled from a duodenal ulcer.

*Dr. Rousselot:*—We are going to demonstrate such a case by esophagram and venogram shortly.

*Dr. Liebowitz:*—As a point of interest is the case reported by Blakemore. An anastomotic shunt had been constructed and hemorrhage recurred several years later, not from varices but from a duodenal ulcer demonstrated at necropsy.

One of the problems in patients who have been subjected to a portacaval shunt is the manifestation of a peculiar pattern of signs and symptoms which has been designated as episodic stupor and appears related to disturbances in ammonia metabolism. Dr. Greene has certain convictions on this aspect of the subject.

*Dr. Carl H. Greene:*—I want to emphasize the point that Dr. Rousselot mentioned, that is the importance of hemorrhage in precipitating an episode of hepatic failure. I use the term "hepatic failure" because while we all know the clinical picture presented by such a patient, we are less sure when we come to interpret it. Personally, I am a good deal like the Scotsman who was asked to define "tact". He said, "I dinna know what tact is, but I can tell you what it is not." (Laughter)

The attempt to analyze hepatic failure dates back to Mann's first experiments on the removal of the liver from the intact dog. He found that when he removed the liver from the dog, the dog promptly died from hypoglycemia. Hypoglycemia is one of the factors that may enter into the picture of hepatic failure. When it occurs, it is very important, but it is relatively infrequent. I have seen only three patients, out of several thousand, in whom one could make a definite diagnosis of proven hepatic failure with hypoglycemia, and in which the hypoglycemia was an important factor in the clinical picture.

Mann also showed that an increase in the uric acid in the blood was a characteristic result of hepatectomy in dogs. The metabolism of uric acid in dogs differs from that in man and this change could not be observed in patients.

Bilirubin ordinarily is nontoxic and hepatic failure cannot be correlated with the intensity of jaundice. Bile acids are not the responsible agent and only slight degrees of hepatic injury inhibit their formation.

Much work has been done on the association of simultaneous hepatic and renal failure in patients—the so-called hepatorenal syndrome. The present consensus of opinion is that while renal failure frequently occurs in patients with hepatic disease there is no true hepatorenal syndrome. The physiologists have shown that urea formation in animals ceases after total hepatectomy.

Disturbances in protein metabolism in hepatic disease are variable and the picture has been slow to develop. The picture of "meat intoxication" produced by an excess of meat in the diet of dogs with an Eck fistula was the first reported. Minot reported the isolation of guanidine from the blood in cases of hepatic failure and considered this to be the toxic factor. Rowntree, Keith and Barrier introduced the use of ammonium salts and of mercurial diuretics in the treatment of ascites. They noted that in some patients the use of large doses resulted in restlessness, sleeplessness and excitement often with disorientation as to time and place. Similar symptoms had been noted by Frerichs in 1851 following the intarvenous injection of ammonium salts.

More recently we have come to recognize that after a hemorrhage, when the intestine is flooded with protein, or when an excessive amount of meat is ingested, there is a flooding of the system with the products of protein breakdown. In all these conditions, the recent studies have shown there is an excess of ammonia in the peripheral blood. At the same time symptoms of disturbances of the central nervous system appear and this particular group of symptoms, I think, are the symptoms of ammonia poisoning.

Ammonia poisoning, with increased ammonia in peripheral blood can develop in three ways: first, a flooding of the system with ammonia, either from ammonium chloride or from too much protein in the intestine; second, from a shunt that takes blood around the liver, so that the liver is unable to convert the ammonia to urea, as is normally done; and, third, from hepatic failure and an inability of the liver to convert ammonia to urea.

I think we must recognize these differences in mechanism whereby ammonia poisoning may develop because of recent studies, such as are reported this morning of the value of glutamic acid in the treatment of ammonia poisoning. They are illuminating and worthwhile, but one of the things emphasized was the irregular effects of treatment. I suspect that glutamic acid will be of most value in the treatment of ammonium poisoning from the flooding of the system with ammonia through a shunt, or from too large doses of ammonium chloride, and less effective in those cases in which the increase in the blood ammonia is a measure of hepatic failure.

I had a patient this last month who demonstrated this. She had ascites, on the basis of an old cirrhosis. She had a cold and had recently had an acute flare-up of hepatitis. I was giving her ammonium chloride to control the ascites, and she developed unconsciousness and mental confusion which promptly dis-

appeared when the ammonium chloride was stopped. Three days later she had a relapse, and at that time we found the blood potassium was 7 mEq. By forcing fluid and sodium we were able to bring back the potassium level to normal, but she went on and died from hepatic insufficiency.

So it is my opinion that while we know a great deal more than formerly about some of the factors that enter into the clinical picture associated with hepatic failure, particularly the importance of ammonia, we do not know the whole story and it cannot be explained on any one specific disturbance. So far, when the physiologists take a liver out of the dog, they can keep the dog alive for 24 to a maximum of 36 hours, and then the dog dies in spite of any treatment. When they can tell us why the dog finally dies and how to prevent this we will be much further along in our interpretation of the clinical picture associated with hepatic failure.

Again I want to stress here the precipitating factors. Failures can be precipitated by stress. Ethyl alcohol in excess will do it. Intercurrent infection will do it. Any operative procedure, not necessarily a portacaval shunt, will do it. Hemorrhage will do it. So we are up against the problem of protecting our patient in every way possible.

I should like to ask Dr. Rousselot two questions. He has stressed the importance of portacaval shunts in acute hemorrhage. I should like to have him define a little more clearly how acute and severe that hemorrhage has to be to justify operation, the first hemorrhagic episode, or only for a hemorrhage of stated severity? I should also like to ask him whether he considers splenectomy a desirable accompaniment of a portacaval shunt?

Dr. Will Mayo used to make the statement that doing a splenectomy would cut down the circulation in the portal vein by a quarter. I have never been able to find out on what basis he made that statement, and I assume it was made on the basis of the relative size of the splenic artery in relation to the size of the celiac axis, but I don't know. I wonder if Dr. Rousselot, when he gets to it, would come back to that question: Does splenectomy produce a significant reduction in the portal blood flow in these cases of portal hypertension?

*Dr. Liebowitz:*—The mechanism of ammonia intoxication is subject to some controversy. The work of Summerskill and associates on one hand show that an hepatic disturbance is at fault, and on the other, that blood is shunted away from the liver through portacaval shunts, natural or surgically contrived. Dr. McDermott gives an incidence of ten per cent of ammonia intoxication in shunted patients. Dr. Rousselot, do you think this estimate too high?

*Dr. Rousselot:*—Yes, I do, Dr. Liebowitz. We certainly haven't seen it in excess of two to three per cent, and our own experience has been such that we have seen it in individuals who have never had surgical procedures. We have seen it in individuals with portacaval shunt, and we have seen it in an individual

with splenorenal shunt, so it is very difficult to indict diversion of portal blood flow as the sole element in initiating this condition.

I know you are going to bring out the recorded case of McDermott, I think it was, in which he did a resection of the head of the pancreas, and because of extension into the portal vein, was obligated to do a portacaval shunt, and the patient subsequently died of hepatic coma due to ammonia intoxication. It is my understanding that he laid it entirely to the portacaval shunt. It may well have been in this particular individual there was no collateralization, as occurs in the average case of portal hypertension.

I think that this is an important fact. You will see in our portovenogram that the patient with portal hypertension, a clinical bleeder, has, over the years diverted a large mass of his portal blood flow, and the experience has been that as much as 80 per cent of portal blood flow was diverted from the liver. This case has been reported, and we also have the animal experiments in dogs with normal livers and without extensive collateral flow, but I do not think those are valid.

I feel a little bit as Dr. Greene does, that it may well be a stress factor rather than a diversion of a small percentage of blood at the time of the surgical procedure.

*Dr. Liebowitz:*—Ammonia intoxication has followed the administration of ammonium chloride, carboresins, and a high protein diet. Caution must be exercised in prescribing these agents to the cirrhotic individual. A practical point that is not generally known is that an appreciable amount of ammonia can be administered in bank blood used for transfusion purposes. Dr. Cincotti and associates have performed a notable service in this regard. Let me quote from their work. "There is a roughly linear progressive daily increment of some 35 gamma per cent ammonia nitrogen up to the 21st day of storage at which time the mean content approximates 0.9 mg. per cent which is 2-3 times higher than ammonia levels seen in impending or overt ammonia intoxication." Hence when bank-blood is given in appreciable quantity, considerable amounts of exogenous ammonia is administered. They cite two cases of bleeding esophageal varices in cirrhotics who received in excess of 10 units of blood. The calculated ammonia administered averaged 4,400 gamma, that is, roughly levels of 360 gamma per cent. Both patients lapsed into coma. These investigators point out that when fresh blood is drawn into a preservative of a sodium glutamate mixture, there is a less steep rise in stored blood ammonia.

Radiographic delineation of the portal system has become an important diagnostic feature in patients with portal hypertension. Dr. Rousselot and Dr. Ruzicka have pioneered in this field, and I might say, immodestly, have performed some rather exquisite studies. This subject will be taken up by Dr. Ruzicka and in turn by Dr. Rousselot.

*Dr. Ruzicka:*—Portal venography was the second method of roentgen study, as you will recall from the first part of the discussion, for demonstrating varices, and studying portal bed block. It is generally accepted as a much more satisfactory method for showing the presence of varices, although perhaps a little more complicated one. Its accuracy is not actually established, although it is presumed that when varices are present, and blood is flowing into them, that they will be visualized by the portal venogram in a very high percentage of cases. This, of course, would be influenced somewhat by the streaming phenomenon. Blood coming from various tributaries of the system often tends to run in a particular stream for a variable distance before admixing with blood coming from another direction or directions. As a result it is theoretically possible not to demonstrate varices in the esophagus in a particular portogram though these may be present.

For example, if we have a stream of blood coming from the superior mesenteric vein through the portal vein to the liver and another from the splenic vein to the portal vein to the coronary vein arising from the portal vein, and the injection were made in the superior mesenteric vein, the opaque medium would go directly through the portal vein to the liver and not visualize the coronary vein and esophageal varices. If, however, the splenic vein were injected, the opaque medium would go into the coronary vein, and then into the esophageal varices. Thus the streaming phenomenon could influence visualization of the varices in esophagus in such a situation. Practically speaking, however, some admixture of the streams might be expected so that some visualization of the esophageal veins even in the above case would be likely, especially when there is a considerable blood flow over them. In general it is felt that the accuracy of the examination is high in demonstrating esophageal varices.

Besides its use in the roentgen demonstration of varices, the portal venogram is a practical and useful aid in the surgical planning of the therapy of portal hypertension. Dr. Rousselot will later show the application of the portal venogram to the clinical problem.

I should like to spend a few moments on the fundamentals of interpretation.

The portal venogram might be defined as the roentgen visualization of the portal venous system. It shows the anatomical picture and permits differentiation between extrahepatic and intrahepatic types of block. Extrahepatic block as in cavernomatous transformation of the portal vein, or as with adjacent mass such as carcinoma of the pancreas, is present when some vein of the portal system outside of the liver is obstructed. Collateral veins are practically always demonstrated in portal block and we shall have more to say about these important structures in a few moments.

(Slide) This slide is a schematic drawing of the portal venous system, simply to refresh your memories as to the anatomical structure. You recall that

the splenic vein and the superior mesenteric vein are the major trunks which join to form the portal vein, and the major tributaries are the coronary vein and the inferior mesenteric vein. Draining into the splenic vein are the pancreatic veins and the gastroepiploic vein. The gastrocolic trunk drains into superior mesenteric vein. Arising from the coronary vein are the esophageal veins, and another vein, the fundic vein, which extends over the fundus of the stomach and then down to join one of the short gastric veins which again enters the splenic vein, in turn. This is simply a diagramatic representation and there may be variations of the scheme.

(Slide) This again is to emphasize the major vessels we deal with in the portal venogram—the splenic vein, and the superior mesenteric vein, and the major tributaries; the inferior mesenteric vein may enter the superior mesenteric vein or may enter the splenic vein or the crotch between the two. The coronary vein may enter the portal vein or the splenic vein or the crotch between the two.

(Slide) This is a postmortem venogram. We performed venograms in the living and found we were quite confused in our attempts at interpretation. Therefore we performed 50 postmortem portograms in the normal. This gave us some basis for understanding the abnormalities. Here we see the portal vein, splenic vein, superior mesenteric vein, and its many branches. Here is the inferior mesenteric vein and here the coronary vein. Here are the very small esophageal veins; when these veins are more than 1 mm. in diameter we consider them dilated.

(Slide) This I present to indicate the types of portal venograms that may be performed. The major examinations are the splenic portogram and the portal portogram. The splenic portogram is a portal venogram in which spleen is injected, and the portal portogram is a portal venogram in which one of the tributaries of the portal system is injected. This might be the inferior mesenteric or the gastroepiloic, or a branch of the superior mesenteric vein, and, of course, laparotomy is required for the injection.

We rely chiefly on the percutaneous splenic portogram but attribute great importance also to the portal portogram. It is our opinion that some of the incomplete visualization caused by streaming can thus be avoided when injections from two different points are made. You will notice that the dye flow is in the direction of the blood flow, that is, hepatopetal, in the normal. When the opaque medium is seen in any vessel that is not in the course of the blood flow toward the liver, it is then that we consider that we have an abnormal venogram. Of course, we expect a small amount of reflux but, aside from this, any vessel that is visualized other than that in the course of blood flow, is presumably acting as a collateral or in a collateral system.

(Slide) This is a transcapillary portogram. The aorta is injected and x-ray exposure is made, when the opaque arrives in the portal venous system. This

theoretically would visualize all of the branches of the portal system, since the opaque material has to pass through the entire capillary system, first the arterial and then the venous and then enter all of the portal tributaries. Practically speaking, there is much dilution of the opaque medium although serial exposure might bring it out satisfactorily.

Still another technic is the transhepatic portogram. In this, opaque medium is injected into the liver. Placement of the needle is similar to that performed in a liver biopsy. Visualization is limited chiefly to intrahepatic branches. It would take injection into a vein into which there was hepatofugal blood flow to visualize more of the system. This method would also be impractical in obstruction of the extrahepatic type.

(Slide) This is an example of a percutaneous splenic portogram. We consider it an examination which should be done with great care and only after considering all the indications and contraindications. Dr. Rousselot stated explicitly that we are dealing with a serious problem in portal hypertension and therefore a more serious type of examination, although it may entail some complications, is justified. We recognize the possibility of splenic hemorrhage, and for that reason certain precautions are observed.

To avoid splenic hemorrhage, the patient is trained before the examination is actually carried out, if the patient is to be awake during the examination. He may be in the x-ray department or in the operating room immediately before surgery. If, of course, the patient is under anesthesia, then the anesthetist helps greatly in the procedure. If the patient is under anesthesia, apnea is induced by the anesthetist during the placing of the needle. Then, afterwards, the patient is allowed to breathe shallowly. If he is awake the patient is instructed to hold his breath during insertion of the needle. After placement of the needle, the patient is permitted to breathe shallowly but holds his breath during the time of the injection. If a series of exposures is made, the patient may be allowed to take an occasional short breath, shallow always, at certain intervals. When the needle is withdrawn again, the patient must hold his breath in order to avoid tearing of the splenic capsule. It is important to obtain a free flow of blood from the needle to assure proper placement of the tip. Usually the ninth interspace is selected, insertion of the needle being made in the axillary or, with small spleens, in the posterior axillary line.

We employ a plastic tube between the needle and syringe, thus avoiding a rigid system and allowing the needle to move freely with the spleen during respiration. Twenty to 40 c.c. of Urokon varying in concentration from 50 to 70 per cent, depending on size of the individual, is injected. Injection is completed in about seven to ten seconds. We use a No. 18 needle. It is important that the needle point be sharp.

I should state that in preparation for the examination the patient is given Demerol one hour prior to examination. Twenty-four hours prior he is put on

neomycin to avoid any possibility of peritoneal infection should the needle be accidentally inserted into the colon. We have never had this occur.

(Slide) This is an example of a normal splenic portogram. You see only those veins in the course of the blood flow toward the liver, that is the splenic vein, the portal vein, and the intrahepatic portal branches.

(Slide) This is a normal portal portogram. Here is a catheter inserted into a small branch of the superior mesenteric vein. There is a small amount of reflux, but the major part of the material flows through the superior mesenteric vein, and the portal vein, to the liver and into the intrahepatic branches of the portal vein. It is a hepatopetal blood flow, which is normal.

The streaming phenomenon is seen in this particular examination. Here is a partially, opacified stream, with resultant streaking in superior mesenteric and portal veins. In the liver there is another manifestation of the streaming phenomenon. You will note that more of the branches of the right intrahepatic branch of the portal veins are filled than the left. Dye flow follows blood flow and these findings indicate incomplete admixture of various blood streams originating from various tributaries.

(Slide) This is a rather difficult subject to expound upon in so short a time and I hope you will bear with me in this detail.

For an understanding of the abnormal physiology of portal obstruction, we must discuss two important pathologic anatomical features, the site of the obstruction and collateral vein development.

The site of obstruction in portal hypertension is of considerable importance. The well-established division of portal obstruction into intrahepatic and extrahepatic types may be used in our understanding of the roentgen findings.

The extrahepatic obstruction we have already had reference to. The intrahepatic obstruction is due to liver disease, and that means, usually, cirrhosis. In this situation major veins leading to the liver are visualized. In extrahepatic obstruction the site of obstruction is often quite well shown by the portal venogram.

With respect to collateral veins, one of the most important findings in the presence of portal obstruction is a demonstration of the collateral veins. Indeed appearance of the collateral veins is a definite indication of portal obstruction and also indicates, according to Atkinson, Sherlocke, and others, portal hypertension; as a matter of fact, they found no case with collateral vein development which did not have portal hypertension.

I should like to show you at this point examples of the more common types of collateral veins that we encounter.

(Slide) This is a coronary gastroesophageal collateral. The coronary vein arises from the portal vein and extends upward along the lesser curvature of the stomach. We then see the varices along the stomach, extending up along the esophagus. These are tremendously dilated veins. In our living material, we have found that all of our cases have had gastric varices, whereas most but not all have esophageal varices demonstrated by this method. This may help clarify your question, Dr. Leibowitz, with regard to reports of demonstration of gastric varices in high percentage by barium study.

As I say, in our material 100 per cent of surgical cases showed gastric varices, whereas only about three-quarters showed esophageal varices. The converse of this, namely, that all cases with esophageal varices also had gastric varices we also found to be true. Therefore, in answering the question as to whether or not the barium method is effective in demonstrating gastric varices, the observer would probably be correct in diagnosing gastric varices regardless of the roentgen findings when esophageal varices are also shown to be present.

(Slide) I should have stated that the previous slide was a case of cirrhosis with intrahepatic obstruction. This is a case of extrahepatic obstruction due to carcinoma of the gallbladder. The obstruction is indicated by the absence of any normal appearing portal vein which is obliterated by the carcinoma. We have here what could be a displaced portal vein, but more likely is a bridging collateral (and several such bridging veins appear to be present) extending from the superior mesenteric vein to the liver, and carrying a hepatopetal blood flow. Other collaterals demonstrated are this pericardiac vein and this diaphragmatic vein. The latter arises from the splenic vein. Here, incidentally, are esophageal varices seen in an esophagram but not too well demonstrated in this study due to technical reasons.

*Dr. Rousselot:*—The barium study in this case shows the postbulbar narrowing of the duodenum and superior aspect by the extension of the tumor.

*Dr. Ruzicka:*—(Slide) This is another type of collateral, the second most frequently encountered collateral that we found in our postmortem study of 40 cases of portal obstruction, and also in the living cases.

This is the transhepatic collateral which you see arising in this case from the left intrahepatic branch. It may arise from the right or left branch. The transhepatic collateral, we think, is an important vein. We have found it carrying blood to the liver, and away from the liver, depending on the type of obstruction, that is, intrahepatic or extrahepatic. In the former, blood flow is usually hepatofugal over the transhepatic vein and in extrahepatic, hepatopetal. In this case the transhepatic extends down toward the hypogastric vein. We see this vein extending in various directions, e.g., to the coronary vein, the vertebral plexus, to the adrenal veins, or to a plexiform retroperitoneal plexus, to mention some of the possibilities.

(Slide) This is a frequently encountered collateral we have seen—the transplenic collateral. You see the splenic and portal veins, some streaming, with incomplete admixture of blood with the opaque medium. The collateral in this case goes from the spleen down towards the hypogastric plexus.

We have encountered a number of other collaterals which I will not talk about, since the time is running short but I should like to emphasize that this whole idea of collateral veins is a developing one, and one where we perhaps may discover many of the secrets of portal bed block, and perhaps even arrive at some information which will help in treatment planning.

*Dr. Liebowitz:*—Dr. Rousselot will now take up the application of venographic demonstration of the portal system in the planning of a surgical procedure designed to correct hypertension.

*Dr. Rousselot:*—Time is running out and so I will ask you to bear with me if I proceed a little rapidly.

(Slide) To preface this series of slides, we would like to reiterate that we believe that the best definitive surgical treatment for bleeding esophageal varices, in the order of importance, is as follows:

1. portacaval shunt;

2. splenorenal shunt;

3. so-called makeshift shunt, untilizing smaller caliber vessels, but of necessity we believe they should be vessels exceeding, 1 cm. in diameter, and if no such vessel is available in the portal bed, then there should be an alternate adjunctive type of surgery with excision of the "critical area" carried out.

This first slide represents a schematic drawing of a splenogram which we will show you shortly, and illustrates an extreme case, showing the wide extent of the varix bed from the esophagus well down into the antral area. It shows the coronary vein, which, as Dr. Ruzicka said, is present in 100 per cent of our clinical bleeders. It also shows the usual position of this vessel and its contribution to collateral blood flow.

I will answer one question which Dr. Greene posed, about Dr. Will Mayo's statement that splenic blood, in congestive splenomegaly, represents approximately 25 per cent of portal blood flow. Some individuals have said it is as high as 40 per cent. I think the contribution of the spleen will depend entirely on the size. We know in some cases the spleen is only moderately enlarged, and in other cases it may reach extreme proportions. Regardless what its contribution is, 10 per cent or 40 per cent, I think it is perfectly obvious why it is that removal of the spleen proved to be so utterly ineffective for esophageal hemorrhage in years gone by, because as soon as the spleen is removed—you get a detour of your entire portal bed flow, and principally here (indicating). If this is present, as it is in 30 to 40 per cent of the cases, it promptly recurs.

(Slide) This is a case that Dr. Ruzicka showed of a 52-year old alcoholic. It demonstrates the small size of the splenic vein,—though he has splenomegaly. It shows that each case presents a different problem, and we feel it is extremely important to have roentgen support in our routine operative management. It is as irrational to proceed with your surgery in this field without localization of the pathology as it is to attempt to perform either pulmonary or bowel surgery without collateral x-ray studies.

So with this small vein here, a splenorenal shunt would be extremely undesirable in this case. A portacaval shunt would be the operation of choice.

(Slide) This is a 23-year old woman with Laennec's cirrhosis. This is the slide from which the schematic drawing was made. Note the takeoff of the coronary, and how far the gastric varices can extend. This is beautifully illustrated, and that drawing was not made from imagination. There is some streaming here such as Dr. Ruzicka mentioned, and in this case, again, a portacaval shunt would give us the biggest runoff and the biggest drop in pressure. The larger the anastomosis is, the larger the drop and the greater the increase in effectiveness of the procedure.

(Slide) A 52-year old alcoholic cirrhotic. This is also another slide Dr. Ruzicka showed you. Here, again, the portal vein, and I may add that we are learning that the portal vein is not always patent (that in cirrhotics anywhere from 11 to 20 per cent can have accompanying bland thrombosis of the portal vein) which, if not known ahead of time, would lead to an inoperable situation. We have encountered these situations such as referred to in other clinics, where the patient had an unnecessary operation and nothing definitive was performed, because the surgeon was not aware of that situation ahead of time.

(Slide) This is an individual 32 years of age, with a posthepatitic cirrhosis, following yellow fever vaccine in 1943 in the Army, and recurrence of hepatitis eight years later, and 13 years after the initial dose, with massive hematemesis. He was traveling in Europe and had his hemorrhage in Warsaw. At laparotomy, thinking they had bleeding ulcer, it was found he had cirrhosis and splenomegaly, and a splenectomy was done. He promptly had a recurrence of his bleeding and was barely able to come back to this country. At operation, since he had no spleen, we could not do a splenic portogram, therefore, we did a portal portogram. A large patent portal vein allowed for a portacaval shunt.

(Slide) This is to illustrate an instance of association of ulcer in a case of cirrhosis in a man known to have Laennec's cirrhosis, and when this picture was taken this demonstrated varices. He had had a subtotal gastrectomy for ulcer, a year and a half prior to this. At that time it was noted there was no bleeding from varices, but there was from his ulcer. This picture and the subsequent splenic portogram were taken from an individual who had had two-thirds of his stomach removed. This demonstrates varices.

(Slide) This is a splenic portogram which shows how recollateralization will develop following a gastric resection, (where the coronary vein is routinely excised) so that this individual one year and a half later had developed collaterals over this route that re-fed these varices. In this patient we were able to do a portacaval shunting.

(Slide) This is a 29-year old cirrhotic, and it is presented just to show the streaming phenomenon with the linear areas of rarefaction. He was a postplenectomized case. He had a splenectomy about a year before we saw him, followed by recurrence of bleeding.

(Slide) The previous group all represented cases of intrahepatic blocks. The next series will all be representative of extrahepatic blocks and congenital extrahepatic blocks.

This is a case of a 34-year old woman who previously had a splenorenal shunt, (one of our own failures). She had protection, with no bleeding, for approximately three years, and then rebled, and at the second operation the portal portogram demonstrated no real tubular portal vein, but the oval areas of rarefaction and a definite lack of definition of the walls of the portal vein. This was indicative of intraluminal thrombosis.

In this case we had no vein large enough available to do a shunt, and we performed an esophagogastrectomy.

(Slide) Another failure. We don't have all failures, but it is only fair to show them. We are illustrating them also as evidence in our mind that a reasonable percentage of splenorenal shunts are going to close off as the years go by.

This is illustrative of a noncirrhotic lad on whom we first operated in 1952, age, 25, normal liver. When we started our splenoportograms we saw that he had a marked washing-out of dye there, which we interpreted as thrombosis. We did a splenorenal shunt on him and gave him protection for four years. He redeveloped the varices then and had a series of severe hemorrhages early this year.

We re-explored him and notice the very marked change in this pattern here. This thrombotic condition had progressed so far there was no longer a visible portal vein structure and we were left with this hepatofugal flow and no vessel large enough to do a shunt. An esophogastrectomy, "adjunct surgery", was done.

(Slide) A 19-year old lad, postsplenectomy, done at another clinic, with recurrence of bleeding. At operation, with the portal portogam, this superior mesenteric vein, we felt, was extremely large, and it was dissected out. Using a vein graft, it was anastomosed to the inferior vena cava. In other words, this represented a so-called "makeshift" shunt combining with the vena cava. He has gone for four years without any recurrence of his bleeding.

(Slide) The next slide again represents an extremely interesting situation in which we elected to do a shunt, after the following history: We did a splenorenal shunt in 1948. He had an extrahepatic block in the upper portal vein. He went eight years with no clinical bleeding. At the end of eight years the follow-up esophagram revealed varices, with no clinical bleeding. We put the problem up to the man, told him the hazards, and he elected to be reoperated on. By this time we were routinely doing portograms.

(Slide) We re-operated upon him and did a portal portogram. This is the obliterated splenic vein stump, and somewhere beyond this was the old splenorenal anastomosis also now obliterated—here is seen a coronary vein. This shows the coronary vein here, and this huge vein was the right gastric vein, which was also easily demonstrated at operation. Since it was a major take-off with great run-off, and was larger than the coronary vein, it was utilized for the shunt. This vein was divided here and swung through an arc of 160° and anastomosed with the inferior vena cava. His follow-up is only for approximately a year and a half (without bleedings) since that second operation.

(Slide) The next three slides are examples of congenital lesions producing extrahepatic blocks. This is a cavernomatous transformation. This is a 10-year old boy and we performed a splenorenal shunt. This and the next chap have gone five and four years, respectively.

(Slide) This represents "agenesis" of the portal vein.

(Slide) This is an extremely interesting case of a six-year old boy, a case with a very unhappy ending. He had repeated hemorrhages over a period of six months, each one being almost exsanguinating. He had normal liver function. Prior to operation, the splenic portogram showed this vessel here, which was extremely tortuous, and made us feel that it represented a curious bridging and probably winding-around of a collateral about the portal vein, with a block somewhere in this area. The coronary vein runs up here, and this was a large gastric varix. The portal vein was not visible. This vein was divided here and swung down to the portal vein.

He had an uneventful postoperative course until he was ready to go home, when we suddenly noticed he was rapidly developing an ascites. The boy went on to a fatal issue of recurring ascites and marked emaciation. We were unfortunate in that we were unable to obtain a postmortem, but our opinion is that in this case we were probably dealing with numerous congenital veno-venous shunts within the liver, and ligating the end of this vessel propagated a thrombus through hepatic substances, with eventual hepatic vein outflow block producing Chiari's syndrome. It represents a very rare case, the only case of its kind that has come to my attention.

In summary, therefore, we feel that the utilization of this new roentgen technic is extremely helpful in diagnosis and surgical planning in therapy of bleeding esophageal varices and portal hypertension.

*Dr. Liebowitz:*—Time is growing short. If there are any questions from the audience we will be glad to answer them, or try to answer them.

*Dr. Ruzicka:*—There is one question here: What is the value of infrared photography?

Well I don't think I can really answer that because I have had no particular experience with it; however, I would say that since it is a means of demonstrating the veins, any collateral veins on the surface which might exist in association with portal obstruction would be well demonstrated. I think it would be a useful adjunct, but it would not tell you much about the portal system proper. It would merely be another method, another confirmation of the diagnosis of portal obstruction.

*Dr. Greene:*—I am going to present a little different point of view on that. For some years back, in fact, I started out with the idea that if one were interested in portal hypertension and the patient had dilated veins in the abdomen, why not measure the venous pressure there, and perhaps get a measure of the increase in the portal pressure. The first few we did were very satisfactory—the patient had ascites, and had obvious collateral veins, and the venous pressure in the collateral veins was increased as compared with the veins in the arm.

Then I made the mistake of doing the venous pressure before tapping and leaving the needle in and measuring the venous pressure after tapping. After tapping, the venous pressure was the same in the veins of the abdomen as in the arm vein. I think that in most patients who have dilated veins over the abdomen, of the kind that are best demonstrated by infrared photography, that this dilatation is the measure of obstruction to the venous flow in the abdominal wall from the pressure of ascitic fluid, and is not a measure of collateral circulation at all.

Now, of course, there is the other group of patients with Chiari's syndrome, and I have seen a few with a true caput Medusa in which there was no question about there being a connection between the portal system and the veins in the abdominal wall. The type of veins that ordinarily show up best by infrared photography represent, not collateral circulation, but only the obstruction to the blood flow in the abdominal wall as a result of pressure.

*Dr. Ruzicka:*—There is one other question here: How many splenograms have you done?

We have done in the neighborhood of 60 injections.

What was the percentage of complications?

This has been low. We have had no major hemorrhage where, e.g., a splenectomy would be necessary.

We know that we have a little bleeding in some cases. We observe them for 24 hours after the splenic injection. We know that perhaps in about 25 per cent there may be some drop in blood pressure during that time of observation: So far as major complications are concerned, however, we have had none. I think there were one or two that could have been serious, but fortunately they were done immediately prior to laparotomy, and the spleen was removed in the course of a splenorenal shunt procedure.

I think Dr. Rousselot might comment on this matter of the complication of bleeding–following splenic injection.

*Dr. Rousselot:*–Yes. We have had no serious bleeding with splenic portography on the service. I know of one case that occurred in another hospital where the individual carrying out the puncture was doing it under general anesthesia and apnea was not maintained. Respiratory motion resulted in splenic tear. This patient was already anesthetized for operation, and the anesthetist commented that the pressure had dropped, and thought it was due to the anesthesia. Rapid exploration was urged, and 1,500 c.c. of blood was aspirated from the peritoneal cavity. That is a definite hazard.

We feel now that by the use of the connecting veno-veno tube between needle and syringe, that if the apnea is not maintained under either general anesthesia or local anesthesia there will be a swing of the needle and no tear will develop.

*Dr. Ruzicka:*–May I ask you how much hemorrhaging there is?

*Dr. Rousselot:*–In the average case never in excess of 100 c.c., and oftentimes it is surprising how little hemorrhage can occur if it is properly done with just the technic and precautions mentioned.

# SELECTION OF OPERATION FOR GASTRIC ULCER*†

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Most of the operations previously advocated for gastric ulcer have been discarded. Gastroenterostomy, with or without local excision of the lesion, was generally found to be unsatisfactory. The symptoms were rarely permanently relieved, and a recurrence either of the gastric ulcer, or the development of a gastrojejunal ulcer, was not infrequent. Sleeve reactions which removed the ulcer are no longer performed because the resultant hour-glass contractions invariably led to serious physiological disturbances. Vagotomy as an isolated procedure, or in combination with gastroenterostomy, has never been popular because not only have recurrences been reported, but some ulcers which clinically were thought to be benign, were carcinomatous. It is now generally conceded that subtotal gastrectomy is no longer the procedure of choice; it is mandatory. This procedure is the only operation at present which satisfies three basic requirements. First it radically removes the ulcer for pathologic examination, for, as Palmer has stated, "there are no diagnostic signs pathognomonic of benignity; on the other hand there are no definite criteria of malignancy". The resected gastric specimen may show instead of a benign ulcer, an ulcer undergoing carcinomatous transformation, a malignant ulcer, or a benign ulcer associated with an independent carcinoma previously unsuspected. Secondly, partial resection removes the pylorus and antrum, the site of the chemical phase of gastric secretion. Following a subtotal gastrectomy of the Billroth II type, 88 per cent of our patients became anacid, which, in our series, probably accounts for the absence of either recurrent gastric ulcer, or a gastrojejunal ulcer because no acid, no ulcer. Thirdly, the majority of patients are free of ulcer complaints and have remained well.

Subtotal gastrectomy, after adequate preoperative preparation, is, therefore, advocated for all gastric ulcers except those which are acute, small, and respond rapidly to medical treatment. It is urged especially for those gastric ulcers producing pyloric obstruction, and certainly for those which are bleeding, and as an emergency procedure in cases associated with massive hemorrhage. In our experience, if these are treated medically, a 25 per cent mortality results. We formerly felt acute perforated gastric ulcers should be treated by a simple suture. We now feel that if the general condition of the patient permits, a subtotal gastrectomy is indicated in most cases.

This is predicated on the possibility that a malignancy may be present or may subsequently develop. Doll reported a series of perforated gastric ulcers

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treated by simple closure in which 8 per cent of the patients who were followed from 2 to 12 years developed carcinoma. This emphasizes the care with which patients who have had a simple perforation of an ulcer must be followed by subsequent x-ray studies.

Technically our method of gastric resection is similar to that which we have described for duodenal ulcer except that it is performed in a retrograde fashion. The duodenum, which is usually freely movable, is divided first, and usually closed without difficulty. Occasionally it is the site of previous scarring, or of active ulceration, because duodenal ulcers may co-exist with benign gastric ulcers. When there is any doubt as to the competence of the duodenal suture, the stump is freely drained through a right subcostal stab incision.

The reason for beginning at the duodenum is that the stomach may be deflected to the left so that an adequate exposure of the posterior wall may be obtained. Occasionally these large penetrating ulcers are firmly glued to the pancreas. In benign lesions, there is no reason to remove part of the adherent pancreas even if it forms the base of the ulcer. Moreover, since the advent of antibiotics, there is no reason to drain this area. Occasionally these calloused perforating ulcers of the lesser curvature are sealed off by the liver and the gallbladder. Many large ulcers, as well as ulcers high on the lesser curvature, may require complete mobilization of the stomach. This is easily obtained by ligating the left gastric artery close to its origin at the coeliac axis, and completely dividing the gastrocolic and gastrolienal ligaments. If necessary, the esophagus may be mobilized by dividing its peritoneal attachments and the branches of the vagus nerve. When this is done, there is little difficulty in removing these high ulcers by subtotal gastrectomy, except those which are juxtaesophageal in position.

Following resection, gastrointestinal continuity may be restored by either gastroduodenostomy, or by a termino-lateral gastrojejunostomy of the Hofmeister type. Prior to 1937 the anastomosis was made posterior to the colon. Since then, we have discarded the posterior retrocolic type of gastrojejunostomy, having been impressed with the simplicity and the technical advantages of restoring gastrointestinal continuity anterior to the colon, using a short proximal loop of jejunum about six inches long. We have noted no difference between this and the posterior anastomosis in either the immediate postoperative period or in the follow-up observation of patients. Enterostomy which was thought to be necessary in high gastric resection for ulcer has been discarded. It was performed only once early in this series.

I should like to mention the Madlener procedure, that is a palliative gastrectomy in which the ulcer is left *in situ*, and a gastrectomy performed distal to the lesion. I realize full well that this operation is highly controversial and open to severe criticism. It is contrary to the accepted theory that all gastric

ulcers should be radically removed. But the "worst use of theory is to make men insensible to fact".

High cardiac ulcers, especially the penetrating variety, may occur in patients who are poor risks and can ill afford to stand the shock of an esophageal and complete gastric mobilization essential to a high gastric resection. And if the lesion is juxtaesophageal in position, in order to remove an esophagogastrectomy a thoracic or an abdominothoracic incision must be done. In the average hands, and I repeat "average", this operation entails an appreciable mortality. If the patient survives, late complications may develop such as difficulty in gastric emptying secondary to complete vagotomy, or the development of a stricture at the site of the esophagojejunal anastomosis. Accordingly for this type of lesion we performed a palliative gastrectomy in 18 patients, all over 50, feeling they were poor risks for extensive operative procedures. In addition, we felt after consideration of their clinical history, their x-ray reports and operative findings, that the possibility of the presence of carcinoma was minimal.

Two died following operation, one from a cardiac complication on the second day, and another from a persistent hemorrhage from a shallow benign juxtaesophageal ulcer. In the survivors, a gastric achlorhydria developed and the ulcer disappeared promptly in all cases as shown by x-ray. Thirteen patients have remained clinically free of symptoms from 3 years to 15 years. One died 6 years later from a nephritis, and an autopsy disclosed a healed gastric ulcer. But, unfortunately, we are not infallible in our judgment. In two other patients in whom the lesion seemingly disappeared by postoperative x-ray examination, carcinoma became evident in one after three years, and in the other after four years, both inoperable at the time of the second operation. In the last patient in whom a postmortem examination was obtained, the pathologist felt that the original lesion was benign and bore no relationship to the present carcinoma. There is nothing to say in extenuation of our mistakes except that often survivors, following a radical operation for carcinoma of the cardia, rarely have a longer or happier life expectancy.

The present surgical management of malignant ulcers has been recently questioned. Most surgeons still perform a subtotal gastrectomy, but only more radical in its extent. It is now routine to remove the major portion of the stomach together with the regional lymph nodes along both the greater and lesser curvatures, the gastrohepatic and gastrocolic omenta, and the proximal centimeter or more of the duodenum. In some instances in which distant metastases are not evident, and in which carcinomatous ulcer invades the tail or body of the pancreas, or nodes are palpable along the splenic pedicle, an *en block* removal of the organs involved is performed.

The only way in which some idea can be gained as to the life expectancy of patients surviving subtotal gastrectomy for malignant ulcer is to group these with other carcinomatous lesions of the stomach which are comparable in size

and extent. In our experience with 348 cases of gastric carcinoma, (1938 through 1947), if the lesion was confined to the stomach and was treated by radical resection, 45 per cent survived three years or more. If the lymph nodes were involved 19 per cent survived three years or more. Our follow-up statistics correspond more or less to those reported by other surgeons. Briefly stated, one-quarter to one-third of patients surviving curative resections lived five years, but when the tumor was confined to the stomach without lymph node involvement, the survival rate was often reported as high as 50 per cent.

These results are not particularly good. A few surgeons have felt that the general principles of carcinoma surgery have not been adequately applied to gastric malignancy. The necessity of total gastrectomy was emphasized by McNeer and Allen because in a study of 120 suitable autopsy protocols of operative survivors who eventually died of cancer following subtotal gastrectomy, about half showed recurrences in the gastric stump, and 15 per cent in the duodenal stump. Their conclusion was that subtotal gastrectomy may have denied the chance of cure to about half of the operative survivors. In order to lessen the possibility of failure, they advocated either a standardized subtotal gastrectomy, or preferably a total gastrectomy. This would entail the removal of the entire stomach with glands, a distal segment of the esophagus, part of the proximal duodenum, and the greater and lesser omenta. It should, according to Allison, include excision of the peritoneum and areolar tissue over the pancreas and up to the inferior surface of the diaphragm, the nodes about the infradiaphragmatic portion of the esophagus, as well as the removal of the spleen and the body and tail of the pancreas.

Whether total gastrectomy is justifiable as a routine procedure depends upon three factors. First, can a true improvement in survival be anticipated? Second, if so, will the higher survival rate be overbalanced by an increase in mortality? And third, is the absence of a stomach compatible with normal existence?

LeFevre and Jacob collected approximately 826 cases of total gastrectomy (1940 to 1950) with an operative mortality of about 20 per cent. As near as could be determined, 10 per cent of 599 patients survived five years or more. While the mortality of total gastrectomy has been greatly reduced in reports of individual operators, it still remains considerably higher than for subtotal resection in comparable hands. The salvage rate at present is low. The total resections in the series referred to were performed in large part for advanced lesions or those involving the cardia. It is not, however, to be supposed that all total resections were done for hopelessly advanced growths. Thirty-five per cent of Lahey's and Marshall's cases had no lymph node involvement, yet only 11 per cent of these were alive five years after operation. Twenty-five per cent of Sweet's cases had no lymph node involvement, and of the 9 cases surviving 3 years or more, 6 were free of lymph node invasion at the time of operation.

It is, therefore, unlikely that any increase in salvage from routine total gastrectomy would be more than offset by the increased operative mortality, and it is even doubtful whether there would be a true improvement in results over those obtained by radical subtotal resection. The amount of stomach removed is not nearly as important as adequate removal of zones of lymphatic drainage. Even with total gastrectomy it is impossible to resect glands behind the pancreas or about the coeliac axis. Cardiac lesions have additional pathways of spread which are often inaccessible surgically. Remine et al, who advocate histologic studies of the edge of the resected stomach and duodenum to make sure that the segment contains all the carcinoma, found no microscopic evidence of involvement in the line of resection either above or below the lesion in 34 patients with gastric cancer and lymph node involvement who survived operation, and who died within a year of metastases.

The final point to be considered is the kind of existence that patients may look forward to without a stomach. There are undoubtedly those who have little digestive disturbance and appear to be economically restored. It has been stated that it is possible for these patients to live useful and active lives with appropriate medical supervision and advice, and as stated by one observer, they "should be considered as problems in medical care as long as they live thereafter". But most of the survivors are miserable. They have little appetite, remain underweight with a persistent anemia due to nutritional disturbance, and suffer from indigestion, the dumping syndrome and dysphagia. In other words, they are invalids until they die.

Ultimate conclusions will depend upon comparisons of mortality, the morbidity, and the three and five-year results in series in which total gastrectomy has been routinely performed for all cases of gastric carcinoma with equivalent series treated by radical subtotal resection.

For the present, however, we agree with many others that radical subtotal gastrectomy should continue to be the operation of choice for malignant gastric ulcers and comparable lesions, reserving total resection for those cases in which the entire or proximal stomach is involved. Following subtotal gastrectomy, most patients have a fairly comfortable existence for at least a few years, and about 25 per cent survive for five years or more. Before surgeons in general are catapulted into this radical removal of viscera in the upper abdomen as a routine procedure, it might have a sobering effect upon them to read the recent invaluable contribution of MacDonald and Kotin. They believe that it is not the type of surgical treatment that determines the end result. It is the biologic predeterminism of the tumor which is the limiting factor of curability. In spite of this, however, there is no reason why we should not try further to improve our present results. These undoubtedly could be bettered if patients with carcinoma of the stomach were brought to surgery earlier at a time when the lesion is confined within the stomach, and has not involved other viscera or metasta-

sized to the glands. This is not a single accomplishment. Its solution provides a fruitful field of research. It is undoubtedly true that the carcinoma may be present for a long silent interval before it causes symptoms. There are, however, cases which are being neglected. Forty-six per cent of our cases had symptoms within 6 months to a year before a diagnosis was made and the operation undertaken. Moreover delay in 13 per cent of our cases was due to the acceptance of a diagnosis of gastric ulcer as an explanation of our symptomatology.

## Conclusions

1. Subtotal gastrectomy is advocated for all gastric ulcers, and as an emergency procedure in massive hemorrhage and perforated ulcers.

2. Radical subtotal gastrectomy is indicated in all malignant ulcers except those which because of their location or extent demand either a total or an esophagogastrectomy.

## Discussion

*Dr. Snapper:*—I have had the privilege of watching the excellent results of Dr. Colp for so many years that I can only say words of praise for his technic and for the care he bestows on his patients. Since I have heard for more than four decades the surgeons always praise their own technic and find fault with the technic of their surgical colleagues, I have become somewhat cautious in my appraisal of surgical technics. The proof of the pudding, however, is in the eating and I gladly testify that Dr. Colp's results are outstanding.

*Dr. O. H. Wangensteen:*—Everyone, I am sure, has enjoyed Dr. Colp's very judicious treatment of this subject. I must confess I have never done a Madlener operation, but I believe that Dr. Colp reasonably could take the point of view that the Madlener principle is involved when one does a segmental gastric resection for duodenal ulcer.

Dr. Colp's displeasure with the segmental operation, I assume, comes from the literature and not from personal experience. Had I been familiar with the literature when I first undertook the procedure, I probably never would have tried it. I knew there was such an operation, but I had never seen the operation done.

The lack of success of segmental resection in the hands of Mikulicz (1897), Riedel (1909, 1912) and Payr (1910) was owing in all likelihood to their failure to appreciate that transection of the stomach vagotomized the segment beyond the site of transverse division. If one adds an adequate pylorotomy, however, of the Heineke-Mikulicz variety, segmental resection becomes a good operation for duodenal ulcer.

Dr. Colp, I assume, holds no special brief for doing the Madlener procedure of leaving the ulcer. Two of his own patients, I believe Dr. Colp said, died later of gastric cancer. It is not difficult to gain access to the attic of the abdomen if one employs the extrapleural lower sternal splitting operation, which incision, together with an upper midline abdominal incision, affords superb, direct and ready access to the lower esophagus and upper stomach. When the juxtacardiac lesion is exposed, it is not difficult to get above it, with the employment of this incision. I prefer definitely to excise the lesion, and if the lesion is found to be benign, a gooseneck-type of repair at the fundic juncture with the esophagus is ordinarily not difficult to complete. In my experience excision of a juxtacardiac ulcer is not a difficult operation. A look at the excised segment of the stomach by the surgeon and the pathologist suffices in most instances to tell whether the surgeon should proceed with a total gastrectomy for cancer; however, a frozen section is mandatory in all doubtful situations.

The judicious things which Dr. Colp said about the surgery of gastric cancer, we all appreciate. It must of necessity be a *complete* operation. I do not think one should ever do a lesser resection for gastric cancer than an 85 to 90 per cent, even though the cancer is at the pyloric canal, because of the extensive lymphatic drainage of the stomach. As technical skills improve, I think that present-day experienced gastric surgeons should be able to do total gastrectomy with a mortality not far out of line with that of the subtotal operation. I agree with Dr. Colp: there is an advantage to the patient to keep a few centimeters of the fundic mucosa, if doing so does not compromise cure of the cancer.

A patient with a total gastrectomy is not a gastric cripple. I have several who have survived for long years, who are able to eat large meals. They all develop a macrocytic pernicious-like anemia. This is an area for fruitful exploratory investigations by surgeons. It has been found in our clinic that patients who undergo proximal gastrectomy, in which only the antral area of the stomach remains—such patients also get a macrocytic anemia after the elapse of 3 to 5 years. It is the fundic segment which protects the patient against development of a macrocytic anemia. In fact, it only takes a few centimeters of fundic mucosa to do so. A patient with only 2 to 3 per cent of the fundic portion of the stomach left will not develop macrocytic anemia. Only that little is necessary to protect against the pernicious-like anemia of total gastrectomy.

I want to register definite and strong objection to the suggestion that patients who have undergone total gastrectomy are "digestive cripples". They are definitely not. Performing total gastrectomies for cancer does, however, impose upon the surgeon and upon his associates—residents, internes, nurses and dietitians in the hospital the task of stressing to the patient the great importance of learning *how to eat*. No patient, after total gastrectomy, should leave the hospital until he is eating reasonably well. Almost invariably, I add a comple-

mental enterostomy for feeding during convalescence when performing total gastrectomy. Feeding the patient through such a catheter helps to restore the appetite. The best stimulus to appetite is to eat—is an old and important saying.

Patients who have undergone either total gastrectomy or complete excision of the acid secreting area of the stomach—all such patients in time develop macrocytic anemia. Fortunately they respond too in the same manner to periodic intramuscular injection of Vitamin $B_{12}$ as do patients with true pernicious anemia. Monthly injections of 30 micrograms of Vitamin $B_{12}$, when the picture of macrocytic anemia develops, suffices to keep the hemoglobin at a satisfying level.

When a patient has gone home and does not do well after a total gastrectomy, I have that patient brought back into the hospital and we concentrate on feeding him. If the enterostomy catheter has been withdrawn and the patient's appetite is not what it should be, a nasal catheter is inserted periodically for drip feedings. Feeding the patient in this manner with a tube will suffice to demonstrate to him that he *can take food,* and once the patient has accepted and mastered that hurdle, everything goes along all right. This is an important precept for all to learn who affect an attitude of interest in the surgery of gastric malignancy.

In doing the dissection for gastric cancer, I would stress the importance and the necessity of doing an adequate lymph node dissection, clearing the hepatic artery and the hepatic vascular pedicle, including the common bile duct.

A timely operation for a gastric ulcer may prove to be an operation for gastric cancer.

*Dr. Ralph Colp:*—I think you are prejudiced against surgeons.

I have known Dr. Snapper for a long time, and I learned this, that he is more right when he is wrong than I am right when I am right, therefore, I try to stay away from any controversial ground.

Dr. Wangensteen's ideas, which you have heard, are good, but I think the interesting thing is that in a country like this we all have our own ideas and should continue to have them, and each go along our own way and publish our results, and maybe sooner or later we will be able to arrive at a very definite conclusion.

# THE URINARY LIPASE TEST AS AN AID IN THE DIAGNOSIS OF CARCINOMA OF THE PANCREAS*

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The most frequently employed laboratory tests for pancreatic diseases are the determination of diastase in serum and urine, the determination of lipase in serum, the analysis of the feces, the glucose tolerance test and the secretin test. Yet, except for the secretin test these laboratory procedures are of no great help in the diagnosis of pancreatic carcinoma.

Elevation of the urinary diastase is rare in cancer of the pancreas. In the experience of most clinicians, determination of the serum diastase is also only of little value for the diagnosis of pancreatic carcinoma. An increase of the lipase in the serum has been found more frequently by some observers. Our own experience with the serum lipase test has been disappointing. Analysis of the feces is important, but not particularly helpful in the diagnosis of a carcinoma of the gland. According to Edward Berk an impaired glucose tolerance with a diabetic type of response has emerged, he says, as probably the most valuable single sign pointing to the pancreas in carcinoma of this organ. In our cases with pancreatic carcinoma an impaired glucose tolerance test occurred only in 30 per cent whereas in recurrent pancreatitis we have seen the diabetic type of the curve in more than 50 per cent of the patients.

For about 15 years we have used the secretin test of pancreatic function. I have performed the test in 750 patients. Among those were 83 cases of pancreatic carcinoma. Seventy-one of them showed a diminished response to stimulation with secretin, in 12 patients the response was normal. On the operating table a carcinoma of the body or tail was found in 10 of these 12 patients, and in the remaining two a rather small tumor was localized in the head of the gland. That means in about 85 per cent of our cases of pancreatic carcinoma the result of the secretin test concurred with the findings at the operation. But still it takes me a whole morning to perform one secretin test and in addition a laboratory technician has to labor for several hours to finish the work. A new test as an aid in the diagnosis of pancreatic carcinoma, may, therefore, be considered as very helpful.

Two years ago Pratt, Callow and I were able to show that a fat-splitting enzyme is present regularly in the urine of dogs. We presented evidence that

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the fat-splitting enzyme is of pancreatic origin, inasmuch as: 1. Injection of mecholyl and secretin in dogs increases the amount of the fat-splitting enzyme in the urine. 2. Removal of the pancreas causes an immediate disappearance of the enzyme in the urine. 3. Ligation of the pancreatic ducts leads to a marked rise in the excreted amount of the enzyme followed slowly by a decrease to rather low values. 4. Ligation of the ducts, followed by pancreatectomy, causes an immediate disappearance of the high values of the enzyme in the urine. From these findings we concluded that the fat-splitting enzyme in the urine is identical with the pancreatic lipase.

Lipase has also been detected regularly in the urine of man. In 100 healthy individuals its concentration ranged from 0.1 to 0.75 units. This means that after incubation of the urine oil emulsion mixture containing 1 c.c. of urine for 24 hours, between 0.1 c.c. and 0.75 c.c. of N/20 sodium hydroxide have been necessary for the titration of the liberated fatty acids to a pink end-point with phenolphthalein. The value for the concentration of lipase in the urine is, it appears, about the same as the value for lipase in the serum. Values of 1.0 unit and more are considered to be significant increases.

During the last two years we have investigated the possibility of using the determination of the lipase in the urine in clinical tests for the existence of pancreatic disease. The urine of almost 500 patients has been tested for urinary lipase and the findings have been evaluated along with the clinical picture and the laboratory examinations particularly as far as pancreatic enzymes in serum and urine are concerned.

In about 425 cases the values for urinary lipase have been found normal, that is less than one unit. In 63 cases the values have been elevated ranging from 1.0 to 3.25 units. A summary of the conditions where increased values of urinary lipase have been determined includes 5 cases with acute pancreatitis and 12 cases with chronic relapsing pancreatitis. There are 28 patients where organs adjacent to the pancreas were diseased primarily and the pancreas had become involved later. In addition 5 cases of diabetes mellitus showed rather high figures for urinary lipase. Every one of these patients had, in his past history, frequent upper abdominal pains. We assume, that in these cases the diabetes has been caused by recurrent attacks of pancreatitis. In six cases values for urinary lipase were elevated although not expected. But the presence of high urinary lipase figures could be explained by the fact that in addition to the original disease there were other signs and symptoms which pointed to a diseased pancreas.

Five cases of kidney disease with severe renal insufficiency are the only cases where we have not been able to explain the elevated enzyme values on the basis of pancreatic involvement.

There was a small group of 5 patients in whom, according to the clinical picture and other laboratory findings, high urinary lipase values might have been expected but were not found. Since the urine of these patients has been taken at random and mostly examined on only one occasion it is conceivable that with more frequent tests the values for urinary lipase might have been found increased.

Studies on urinary lipase have been performed in 14 cases of pancreatic carcinoma.

The patients were explored in our hospital and in all of them the preoperative diagnosis was confirmed through biopsy. In seven cases the tumor was found in the head of the gland and in seven in the body or tail, a rather high percentage for this localization. All cases showed normal figures for urinary lipase in addition to normal values for serum lipase and urinary and serum diastase. In seven of the patients the examinations were performed almost daily. The only laboratory test which supported the diagnosis of carcinoma was the secretin test. It was done in six cases and disclosed in four cases marked impairment of pancreatic function. In the two cases, which showed normal response to injection of secretin, the tumor was localized in the body or tail of the pancreas. The 14 cases of pancreatic carcinoma showed an extended replacement of glandular tissue with carcinomatous tissue. It is this small quantity of remaining normally functioning pancreatic tissue which may be too small to allow an increase of the pancreatic enzymes either in the blood or in the urine.

The fact that in pancreatic carcinoma urinary lipase as urinary and serum diastase did not show any change from normal and was, therefore, no help for the diagnosis was a great disappointment at least at the beginning of our studies. But it raised the question as to whether the response of urinary lipase to stimulation with secretin might differ in normal cases from cases with carcinoma. This proved to be true.

Patients at our hospital, who were free of gastrointestinal signs and symptoms, were given secretin intravenously and each specimen of urine was tested for urinary lipase for 24 hours or even 48 hours. The first two specimens were collected one hour and two hours after the injection. Then the patients were asked to urinate about every two hours during the day and about every four hours during the night. The patients were kept fasting until two hours after the administration of the drug. With the injection two glasses of water were given to ascertain urine excretion at the wanted time. Secretin Lilly was used and the amount given was 100 units.

In a normal person, about two hours after the injection, the values for lipase in the urine started to rise. The highest figures were reached after 6-10

hours, sometimes even later. Twenty-four hours after the administration of the drug the values were back to normal.

In some cases we determined the values for urinary lipase for 24 hours prior to the injection of secretin not to overlook any changes which may occur during a day. These fluctuations are insignificant.

The response of patients with pancreatic carcinoma to the injection of secretin was completely different. After injection of secretin there was regularly a decrease in the concentration of lipase in the urine which in some specimens may amount even to a complete disappearance of the enzyme.

In some normal cases the values for urinary lipase after injection of secretin have been determined for 48 hours instead of 24 hours. The increase during the first day is followed by a marked decrease of the curve later. The decline on the second day is more pronounced when larger amounts of secretin have been given. The course of the curve on the second day is apparently an expression of a functional if transient exhaustion of the pancreatic gland. It is quite similar to the picture of a carcinomatous patient in the first 24 hours after the injection. We, therefore, are inclined to assume that the response of the carcinomatous pancreas to stimulation with secretin is the expression of an exhaustion of the organ invaded by the carcinomatous growth.

Important from a clinical point of view is the fact that there is no difference in the response to secretin whether the tumor is localized in the head of the pancreas or in the body or tail.

The representation is based on the findings on 12 normal cases, normal at least as far as their gastrointestinal tract is concerned and 14 patients with carcinoma of the pancreas. In addition we have tested 5 cases with recurrent pancreatitis. The response in these patients to injection of secretin is definitely different from the response in normals as well as in patients with carcinoma of the pancreas. The basic levels are higher and there is very little if any response to the injection of secretin. The course of the curve is similar to the curve you have seen before which showed the daily fluctuations of the urinary lipase valves in a normal individual without secretin. The difference is that the curve of the patients with recurrent pancreatitis is on a markedly higher level.

What we may call the urinary lipase test has been performed in 30 persons. The number is still small. It is our hope that the test which I have presented will develop as an important aid in the early diagnosis of the carcinoma of the pancreas.

## Discussion

*Dr. Alfonso A. Lombardi (New York, N. Y.):*—Dr. Nothman and his associates should be congratulated for their presentation. I am afraid they have

covered the subject so well that they have left very little for me to say. The problem of diagnosing pancreatic disease, especially carcinoma, however, has, at times, taxed the most astute physician, and it might be worthwhile to reiterate some of the things already known.

Actually it has been only since the early 1900's that gastroenterologists have explored the physiology and pathology of the pancreas, and great strides have been made since then. The biochemist gave us the methods of determining amylase and lipase activity in the serum and in the urine. With the advent of these determinations it was felt that one could easily differentiate pancreatic disease from other gastrointestinal disorders. We soon learned, however, that the serum amylase level would rise early in the disease and would return to normal within 48 hours or so. The serum amylase level was also found to be elevated in other diseases, such as penetrating or perforating duodenal ulcers, and in uremia, intestinal obstruction, hepatitis, after the administration of opiates, and even after thyroidectomy.

The serum lipase was then felt to be more helpful in the diagnosis of pancreatic disease because it remained elevated longer than the lipase, but it, too, could be found elevated in conditions other than pancreatic disease.

Dr. Nothman and associates have now revived urinary lipase determinations. The most significant factor in this is that the urinary determination of lipase will be helpful when both serum amylase and lipase levels are back to normal. As has been pointed out, however, one must not forget to rule out some of the other conditions that cause elevation in these enzymes.

Recently the universe has rediscovered the atom and its forces, and one would not be considered fashionable if he forgot to mention these "hot" substances. Ruffin and his associates at Duke University have administered radioactive iodine-labeled fat meals to test subjects, and then assayed the radioactive iodine content in the blood and in the feces. By this method they were able to demonstrate that in chronic relapsing pancreatitis the average blood levels were significantly lower than in the normal, and the radioactive iodine level in the stool was definitely higher than normal. The same results were obtained with proven cases of carcinoma of the pancreas. Their method is basically a demonstration of faulty fat digestion and absorption that occurs in pancreatic disorders. It, however, also opens new doors for the study of gastrointestinal physiology.

Again I want to compliment Dr. Nothman and thank him for presenting such an interesting paper.

*Dr. Emanuel W. Lipschutz (Brooklyn, N. Y.):*—We all agree that carcinoma of the body and tail of the pancreas continues to be a challenging problem to the clinician and, of course, any new method which would help in the diagnosis would indeed be very welcome.

When confronted with a tentative diagnosis of carcinoma of the pancreas, with the exception of some of the indirect x-ray findings or signs, the clinician is mainly dependent upon two laboratory procedures. One, as you all know, is the secretin test, wherein the duodenal contents are quantitated for the lipase and amylase and bicarbonates after secretin stimulation. The second laboratory procedure depends upon the examination of the enzymes of the pancreas in the blood serum, either with secretin or without secretin; and, as you know, with various parasympathetic stimulants such as mecholyl and choline. Lately we have been availing ourselves of morphine in addition to secretin and parasympathetic agents so as to block the pancreatic duct and then determine amylase and lipase in the blood. This we thought may help our diagnosis of a pancreatic lesion.

The first test, the secretin test, as you all know, is the most reliable, but unfortunately it is rather time-consuming and requires meticulous care in its performance, and because of this it has not been used often enough.

The second procedure, regarding the determination of blood amylase and lipase, we have found, is not too consistent in results, so much so that we have not been able to really establish any specific criteria for the diagnosis of pancreatic carcinoma.

Dr. Nothman has presented a very interesting paper and some very convincing and impressive figures and facts and, as I said before, we certainly are interested to avail ourselves of this method in the near future.

I want to thank Dr. Nothman and compliment him on his excellent presentation, and assure him it was a privilege to discuss the paper.

*Dr. M. M. Nothman (Boston, Mass.)*:—I want to thank the discussers for the kind words about the work of our group in Boston. We started our investigations because all the other procedures which are or have been available for the diagnosis of pancreatic carcinoma have not been satisfactory enough. I hope that with the urine lipase test—not just determination of the lipase in the urine, which would represent only little help for the diagnosis of the carcinoma as compared with other pancreatic tests in urine and serum—progress will be achieved. When I say the urinary lipase test I mean the determination of the lipase in each sample of urine which we get after injection of secretin for 24 hours. In our studies, the curves of cases with carcinoma have shown a marked difference compared with the curves of normals, and also with the curves in five cases of recurring pancreatitis.

I hope that the test will help us medical men to make the diagnosis of carcinoma of the pancreas earlier, so that the surgeons will get the cases in time to operate successfully, and not as it so often occurs when it is too late.

# STEATORRHEA*

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Steatorrhea is the term applied to the condition associated with the excretion of excessive fat in the feces. Stool fat content in excess of 10 per cent of the amount ingested is considered abnormal[1]. Electrolyte and metabolic derangements, resulting from this excessive loss of fat, may produce similar symptoms in diseases of varying etiologies.

It was therefore decided to evaluate the clinical and laboratory manifestations of the disease entities having the common factor of steatorrhea, in order to establish a differential diagnosis. The clinical records of the 46 patients with steatorrhea seen at the Brooklyn Veterans Administration Hospital, Maimonides Hospital, Kings County Hospital and Long Island College Hospital during the past eight years were reviewed.

Steatorrhea may result from any factor interfering with the transfer of fat across the intestinal membrane barrier. Failure of adequate emulsification causes an increase in fecal fat. In this series (Table I), two patients had a significant steatorrhea due to obstructive jaundice. In one, this resulted from stenosis of the common hepatic duct and in the other from cholangiolitic cirrhosis.

Deficiency of the lipolytic enzyme of the pancreas likewise leads to an increased amount of fat, which is predominantly the neutral fraction. Six patients were in this category. One gave a history of fibrocystic disease, one of surgical resection of the pancreas for carcinoma, and four had chronic pancreatitis.

Thirty-eight of the patients studied had defective absorption of fat by the intestinal mucosa. In seven, this was due to intrinsic disease of the intestinal wall. Four patients had segmental enteritis, one had scleroderma, and one had

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amyloid infiltration. One patient had a large multiloculated diverticulum of the jejunum which retained the barium meal for many days. Conceivably, alteration in bacterial flora may have caused changes in fat absorption. The steatorrhea and macrocytic anemia cleared after surgical resection of the diverticulum.

Ten patients had steatorrhea because of an inadequate length of effective intestinal absorbing surface. In two, this resulted from surgical resection and exclusion procedures on the jejunum. Four had fatty stools after gastric resec-

TABLE I

CAUSES OF STEATORRHEA

1. Defects in Emulsification
   a. *Deficiency of Bile Acids* 2
      (Obstructive Jaundice)
      Cholangiolitic cirrhosis 1
      Stenosis common hepatic duct 1
2. Defects in Digestion
   a. *Pancreatic Deficiency* 6
      Cystic fibrosis 1
      Chronic pancreatitis 4
      Pancreatectomy 1
3. Defects in Absorption
   a. *Disease of Intestinal Wall* 7
      Regional Enteritis 4
      Scleroderma 1
      Amyloid disease 1
      Jejunal diverticula 1
   b. *Decrease in Length of Functioning Absorbing Surface* 10
      Surgical resection (or exclusion) 2
      Gastrojejunostomy 4
      Gastroileostomy (surgical error) 3
      Intestinal fistula (jejunocolic) 1
   c. *Disease Occluding Intestinal Lymphatics* 5
      Hodgkin's 1
      Lymphosarcoma 2
      Reticulum cell sarcoma 1
      Intestinal lipodystrophy 1
   d. *Idiopathic steatorrhea*
4. Miscellaneous
      Giardiasis

tion. Three patients had a gastroileostomy performed in error. One patient had a jejunocolic fistula secondary to carcinoma of the colon.

Disease of the intestinal lymphatics interfered with the absorption of fats in five patients. One patient had Hodgkin's disease, two had lymphosarcoma and one had reticulum cell sarcoma. One patient had a diagnosis of intestinal lipodystrophy, established by periodic acid Schiff stain of an abdominal node at another institution.

TABLE II

SYMPTOMS OF STEATORRHEA

| | Defect in Emulsification | | Defect in Digestion | | | Disease of Intestinal Wall (7) | | | | Defect in Absorption Decrease in Absorbing Surface | | | | Disease of Lymphatics | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Hepatic Duct Stenosis (1) | Cirrhois (1) | Cystic Fibrosis (1) | Chronic Pancreatitis (4) | Pancreatic Excision (1) | Regional Enteritis (4) | Scleroderma (1) | Amyloid (1) | Jejunal Diverticula (1) | Resection (2) | Gastro-jejunostomy (4) | Gastro-ileostomy (3) | Fistula (1) | Hodgkin's (1) | Lymphosa (2) | Reticulum Cell Sarcoma (1) | Intestinal Lipodystrophy (1) | Sprue (16) |
| Diarrhea | 1 | 1 | 1 | 1 | 1 | 2 | | 2 | 1 | 2 | 2 | 3 | 1 | 1 | 2 | 1 | 1 | 14 |
| Abdominal Discomfort | 1 | | 2 | | | 2 | | 1 | | | | 3 | 1 | 1 | 2 | 1 | 1 | 15 |
| Abdominal pain | | | | 4 | | 2 | 1 | | | | | 2 | 1 | 1 | 1 | 1 | | 1 |
| Anorexia—Weakness | 1 | | | | | 2 | 1 | | 1 | 1 | 3 | 3 | 1 | 1 | 2 | 1 (late) | 1 | 16 |
| Weight loss | 1 | 1 | 1 | 1 | | 4 | | 2 | 1 | 2 | 3 | 3 (marked) | 4 (marked) | 1 | 1 | 1 | 1 | 15 |
| Anemia | | | | | | | | | | | | | | | | | | |
| Hypochromic | | | | | | 1 | | | | 1 | 1 | 1 | 1 | 1 | 2 | | 1 | 1 |
| Normachromic | | | | | 1 | | 1 | 1 | | 1 | 1 | | | | | 1 | | 7 |
| Macrocytic | | | | | | | | | 1 | | | | | | | | | 4 |
| Nocturnal Diuresis | | | | | | | | 1 | | | | | | | 1 | | | 3 |
| Purpura, Menorrhagia or bleeding | 1 | | | | | | | | | | | | | | | | 1 | 3 |
| Borborygmi | | 1 | | | | 3 | | | ? | | | | 1 | | | | 1 | 15 |
| Tetany | | | | | | 1 | | | | | | | | 1 | 1 | | | 2 |
| Fever | 1 | | 1 | | | 3 | 1 | | | | | | | 1 | 2 | 1 | 1 | 3 |
| Joint Pain | | | | | | 1 | | | | | | | | | | | 1 | 2 |
| Jaundice | 1 | 1 | | 1 | | | | | | | | | | | | | | |

Idiopathic steatorrhea was encountered in 15 patients. This disease must be considered a diffuse malabsorption syndrome. Defect in absorption of glucose, Vitamin A, Vitamin K, Vitamin D, iron, calcium, urea, thiamine and often amino acids has been shown[2].

One patient presented with unexplained fatty diarrhea. The only abnormality found was a massive infestation with *giardia lamblia*. Treatment with atabrine improved the diarrhea but the fecal fat content remained high (14 per cent).

All 46 patients had, in common, symptoms of weight loss, flatulence and increased number of yellow, greasy, liquid or soft bowel movements, the odor of which varied from rancid to foul (Table II). Abdominal discomfort was more often found in patients with frank disease of the intestinal wall or lymphatics. Pain was a symptom in one patient with sprue, but abdominal discomfort was present in the other 15 patients. Those with chronic pancreatitis all complained of pain.

Twenty-nine of the 46 patients had anemia of varying degree. In 10 it was hypochromic, in 10 it was normochromic, and in 5 it was hyperchromic. Four of these latter patients had sprue and one had a jejunal diverticulum with stasis. Four patients with sprue had a normal blood picture. The retention of water in the bowel resulted in a nocturnal diuresis in five patients. Three had sprue, one lymphosarcoma and one amyloid disease.

Hypovitaminosis K is associated with defective absorption of fat and this results in hypoprothrombinemia. Three patients with sprue and one patient with stenosis of the hepatic common duct presented with menorrhagia or purpura. The latter patient was frankly jaundiced.

Calcium is also lost. This resulted in tetany in one patient with advanced segmental enteritis, two with sprue and two with lymphomatous disease of the small bowel. Fever occurred in three patients with segmental enteritis and in five with disease of the intestinal lymphatics. It is interesting to note that three patients with sprue had fever.

A history of childhood diarrhea or celiac disease was obtained in three patients with sprue. The patient with cystic fibrosis of the pancreas had difficulty from the first month of life.

The physical examination suggests the diagnosis of regional enteritis if a mass is palpable, as found in two patients. Frank jaundice with hepatomegaly suggests bile acid deficiency as an etiology of steatorrhea.

Clubbing of the fingers was found in two patients with sprue, two with lymphosarcoma and two with segmental enteritis. The patient with Whipple's disease also had clubbing. Glossitis was found in only two patients with sprue, two patients with segmental enteritis and two with lymphosarcoma. Pigmenta-

TABLE III

PHYSICAL FINDINGS

| | Defect in Emulsification | | Defect in Digestion | | | Disease of Intestinal Wall | | | | Defect in Absorption Decrease in Absorbing Surface | | | | Disease of Lymphatics | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Hepatic Duct Stenosis | Cirrhosis | Cystic Fibrosis | Chronic Pancreatitis | Pancreatic Excision | Regional Enteritis | Scleroderma | Amyloid | Jejunal Diverticula | Resection | Gastro-jejunostomy | Gastro-ileostomy | Fistula | Hodgkin's | Lymphosarcoma | Reticulum Cell Sarcoma | Intestinal Lipodystrophy | Sprue |
| Cachexia | | | | 1 | 1 | 2 | | 1 | | | | 2 | | 1 | 1 | | | 14 |
| Clubbing | | | | | | | | | | | | | | | 2 | | 1 | 2 |
| Glossitis | | | | | | 2 | | | | | | | | | 2 | | 1 | |
| Pigmentation or Skin Change | | | | | | 1 | 1 | | | | | | | | | | 1 | 2 |
| Edema | | | | | | 1 | | 1 | | | | 1 | | 1 | 1 | | | 4 |
| Palpable Mass | | | | | | 2 | | | | | | | | | | | | |
| Hepatosplenomegaly or Nodes | 1 | 1 | | 1 | 1 | 1 | | 1 | | | | | | | 1 | | 1 | 2 |

tion of the skin was found in one patient with regional enteritis, two patients with sprue and the patient with the lipodystrophy. Edema was present in four patients with sprue, one each with lymphosarcoma, Hodgkin's disease, gastro-ileostomy, amyloid disease and segmental enteritis. The serum albumin was low in all patients at the time edema appeared except in the patient with Hodgkin's disease.

Laboratory aid is essential in pinpointing the etiologic basis of steatorrhea (Table IV). The highest fat values (over 30 per cent) were found in the patients with pancreatic disease, lymphoma of the intestines and sprue. In pancreatic disease the neutral fat was more than 60 per cent of the total fecal fat. In sprue the fatty acid fraction averaged 72 per cent of the total. This was the same fractionation found in a patient with lymphosarcoma.

The radiologic examination of the small bowel helps differentiate the malabsorption syndrome from pancreatogenous steatorrhea. In sprue, dilated air-filled loops of small bowel may be seen on the plain film of the abdomen. A true moulage pattern was present in 14 of 16 patients with sprue. Coarsening of the folds, and fragmentation of the barium meal was present in all these patients. Frazer has shown this to be the result of excessive mucus secretion secondary to abnormal amounts of fatty acid in the intestinal content[3]. Only two sprue patients had a normal bowel pattern. All of the patients with pancreatic disease had a normal small bowel except for one man with pancreatitis who had a coarsened mucosal pattern. The transit time was of no significance. In four patients with sprue there was an increased motility, eight patients had normal motility and four had hypomotile intestinal function.

Great difficulty might be encountered in differentiating lymphosarcoma from sprue radiologically. In one patient this was impossible and exploratory laparotomy had to be undertaken to establish a diagnosis.

Osteoporosis of the bones occurred in four patients with sprue. No other condition associated with steatorrhea seemed to produce as great a loss of calcium from the bones.

A very valuable laboratory test is Althausen's starch tolerance test[4]. A flat curve is obtained in both pancreatogenous steatorrhea and sprue. The glucose tolerance curve, however, is high and moderately prolonged in the former condition and flat in the latter.

The Vitamin A absorption curve parallels the absorption of fat[5]. The lowest curves were obtained in the sprue patients. The most prolonged prothrombin times were also obtained in these patients.

Abnormal liver function studies were noted in five patients with sprue, in one patient with ileitis and in one with reticulum cell sarcoma. It is surprising that a greater number of patients with sprue did not show hepatocellular dys-

TABL

LABORATOR

| | Defect in Emulsification | | Defect in Digestion | | | Diseases of Intestinal Wa | | |
|---|---|---|---|---|---|---|---|---|
| | Stenosis Hepatic Duct | Cirrhosis | Cystic Fibrosis | Chronic Pancreatitis | Pancrea-tectomy | Regional Enteritis | Scleroderma | Amyloid |
| No. Cases | 1 | 1 | 1 | 4 | 1 | 4 | 1 | 1 |
| Gastric analysis | *N | N | N | Decrease (2) | N | Slight Decrease (2) | | |
| Fecal fat | 18.9% | 15.2% | 40% | Ave. 36% | 42% | 25% | 20% | 20.6% |
| Fecal nitrogen | N | N | Increase | Increase | Increase | Slight increase | | |
| Oral glucose tolerance | N | N | Increase | High (2) | High | N | N | N |
| Starch tolerance | N | N | Low Peak | Low | Low | N | N | |
| Vitamin A curve | N | Low | Low | Low | Low | N | | |
| Calcium | N | N | N | N | N | Low (2)—5mg., 8mg. | N | |
| Phosphorous | | | | | | N | | |
| Alkaline phosphatase | High | High | N | 16 K-A Units (1 case) | N | N | | |
| X-ray small bowel | N | N | N | Abnormal | N | Stenosing ileitis | Rigidity, dilatation | Coarsened pattern |
| X-ray bones | N | N | N | N | N | | Osteoporosis, hands | |
| Prothrombin time | Moderate elevation | Moderate elevation | N | Slight elevation | N | N | N | |
| Serum protein | N | Slight Decrease | N | N | N | Low (2) | Low | |
| Liver chemistries | N | Abnormal | N | N | N | Cephalin flocculation (1), 2+ | | |
| Potassium | | | | | | | | |
| Water tolerance | | | | | | | | |
| Biopsy | | | | | | | Skin positive | Liver positive |

*N—Normal

V

INDINGS

| | Defect in Absorption Decrease in Absorbing Surface | | | | Disease of Lymphatics | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Jejunal Diverticula | Resection | Gastro-jejunostomy | Gastro-ileostomy | Fistula | Hodgkin's | Lympho-sarcoma | Reticulum Cell Sarcoma | Whipple's Disease | Sprue |
| 1 | 2 | 4 | 3 | 1 | 1 | 2 | 1 | 1 | 16 |
| Low | N | | | | N | N | N | N | Absent—1, Low—4, Normal—7 |
| Increased | 16% | 14% | 18% | Increased | 26% | 18.4%; 33.9% | 18% | 40% | 30% (10) |
| | | | Increased | Increased | N | N | | | Increased (2) |
| N | N | | N | | N | N | N | N | Flat |
| | | | | | N | N | N | N | Flat |
| | N | | Low | | T | Low, flat | | | Low |
| | | | | | 6.2 | 8.6 | | | 8 (7) 6 (2) |
| | | | | | | | | | N |
| | | | | Elevated | | | | | Elevated |
| Large diverticulum | Diagnostic | Diagnostic | Diagnostic | Diagnostic | Multiple defects | Sprue-like | Dilatation | Hypermotility | Dilated loops, (10), Moulage (4), Normal (2) |
| | | | | | N | N | | | Osteoporosis (4) |
| N | Elevated (1) | | Elevated (1) | | | | Elevated | Elevated | Elevated (11) |
| Low | | | | | Low albumin | | | | |
| | N | N | N | | | Abnormal BSP | Abnormal | | Abnormal (5) |
| | | | | | Low 2.4 | Low 1.9 | N | N | Low (3) |
| | | | | | | Positive | | | Positive |
| | | | | | | | | | |

function. The debility and malnutrition of this disease would be expected to produce liver damage.

## Comment

No great difficulty is encountered in establishing the fact that steatorrhea is secondary to obstructive jaundice or disease intrinsic to the intestinal wall or resulting from surgical procedures. More of a problem is the differentiation of other causes of steatorrhea. A well nourished individual with a history of recurrent abdominal pain is more likely to have chronic pancreatitis than sprue. The finding of pancreatic calcification, a low starch tolerance curve and high or normal glucose tolerance tends to make the diagnosis. Most difficulty encountered is in differentiating lymphoma of the intestine from sprue. Since recent advances in chemotherapy and in radiation therapy affords some hope of salvage early diagnosis is important. It may be necessary after all tests are evaluated to resort to laparotomy in order to establish the diagnosis of lymphoma.

## Summary

1. The causes of steatorrhea in 46 patients encountered in the past eight years are reviewed.

2. The similarity of clinical symptoms in varying clinical entities is emphasized.

3. The importance of differentiating the etiologic factors producing the steatorrhea bears emphasis.

## REFERENCES

1. Cooke, W. T., Elkes, J. J., Frazer, A. C., Parkes, J., Peeney, A. L. P., Sammons, H. G. and Thomas, G.: Quart. J. Med. **39**:141, 1946.
2. Comfort, M. W., Wallaeger, E. E., Taylor, A. G. and Power, M. H.: Gastroenterology, **23**:155, 1953.
3. French, J. M.: Modern Trends in Gastroenterology, Edited by F. Avery Jones, Chapter 21, Page 526, Paul Hoeber & Co., N. Y., 1952.
4. Althausen, T. L. and Uyeyama, K.: Ann. Int. Med., **41**:563, 1954.
5. Legerton, C. W. Jr., Texter, E. C. and Ruffin, J. M.: Gastroenterology, **23**:477, 1953.

## Discussion

*Dr. L. Pulsifer (Rochester, N. Y.):*—First may I sincerely compliment the authors on their splendid piece of work and thank them for the detailed observations they have given us. They certainly are to be congratulated. After hearing the excellent symposium this morning, and now listening to this very high-grade paper one is left very little to say. About one-third of the cases that they presented, however, were those of idiopathic steatorrhea and perhaps I can make some worthwhile comments on this condition.

I should like to ask Dr. Fierst if he saw any of his cases before they became sick enough to be hospitalized. Shouldn't some of these reported have been recognized as suffering from steatorrhea and so hospitalization avoided? One might deduce that it is not a very common condition in hospital practice since these gentlemen found only 16 cases in eight years' admissions in several hospitals.

Most of us do not make this diagnosis very often in the course of many years of gastroenterological practice. Forced feeding regimens, ulcer diet programs, dietary indiscretions and periods of stress may occasionally precipitate acute steatorrheaic diarrhea in patients who usually exhibit only the milder symptoms of this disease entity, and who do not have the severe malnutrition reported here and in textbooks.

The diagnosis, of course, depends upon the history, examination of stools, the smooth red tongue—which perhaps is not as common as we previously thought—the noisy abdomen, and so on. When these patients are seen in the office, or even at home, we may start the research which should be as extensive as the condition seems to warrant. I dare say it may not need to be too extensive in some cases, now that we have the gluten-free diet to experiment with.

The low fat regime, for idiopathic sprue, is apparently out the window. The gluten-free diet, so far as I could determine by searching English language medical literature, was reported to be used successfully in this condition only as recently as 1952. An article I found was in *The Lancet*, of that year, in which Anderson and his co-workers described remarkable recoveries in celiac disease in children, through its use.

In 1954 there was published in *The New England Journal of Medicine*, an article by Dr. Ruffin, of Duke University, who described the course of recovery of a very, very ill woman, 39 years old, who had been seriously ill with idiopathic steatorrhea for many years. This case is very like the one Dr. Almy told us about this morning. Recovery occurred while the patient was treated essentially with only the gluten-free diet.

When I heard Dr. Monat, of Washington, recommend his sprue diet in ulcerative colitis, yesterday, I noticed that his diet was almost gluten-free. It leads one to wonder how often this malabsorption syndrome, idiopathic sprue, may occur simultaneously with idiopathic ulcerative colitis or whether the two conditions may, in some way, be relatives.

I should like to suggest to Dr. Fierst and Dr. Robinson that they report to us, some other year, on what time does to their 16 cases who now seem to have idiopathic steatorrhea. Will a year's time or a month's time reveal them to have some primary pathologic entity, other than this condition, which is not now obvious? What will have the gluten-free diet done for these cases?

*Dr. William W. Abrams (Kansas City, Kans.)*:—I want to congratulate Dr. Fierst and his associates on the fine presentation of this paper. His outline and discussions of the symptomatology and differential diagnosis of the very numerous conditions producing steatorrhea are excellent. The x-ray pictures that we have seen concerning the various cases showed the numerous conditions that can produce steatorrhea.

Dr. Fierst makes the statement that stool fat content in excess of 10 per cent is considered abnormal. This generally holds true regardless of any large amount of fat in the daily diet; as a matter of fact, fat intake of as much as 150 gm. per day would still show no more than 10 per cent of the intake.

In the group of 46 patients discussed, there were mentioned 10 who had steatorrhea because of an inadequate length of intestinal absorbing surface, as after gut resections, gastroileostomy, ileal resections and the jejunocolic fistulae. That takes into consideration the length of absorbing surface. With this in mind, it is conceivable that a like situation could occur in the ordinary condition of hypermotility of the intestine, where there are rush peristaltic waves, and in which the nutrients are hurried along the gut. These patients, because of the hypermotility, could contain in their stool a larger than normal percentage of fat along with the other items mentioned, such as the unabsorbed sugar, protein, Vitamin K, folic acid, etc. The results, of course, would vary depending on the amount of material absorbed, and there would be different symptomatology and signs of deficiency disease and steatorrhea, accordingly.

In spite of the fact that Dr. Fierst states that the transit time in sprue is of no significance, the etiology of any hypermotility should be investigated. There may be causative factors such as peptic ulcer or stress situations, and/or associated hypoglycemia. Irritating foods and even allergenic foods, including gluten hypersensitivity, may be factors.

The ulcers and other pathological conditions, which are organic, could and should be treated, whether the treatment be medical or surgical. The intake of the irritating factors in the food, or the allergenic factors, should be taken into consideration. They should be lessened or even removed from the diet entirely, if it is possible, and a definitive, proper regime should be instituted which should include the corrective diet plus medications such as barbiturates, tranquilizers, the anticholinergics, and possibly the steroids.

I believe that steroid therapy has great possibilities in treatment of steatorrhea. It should be kept in mind, at least, as a method of treatment.

As was heard this morning in the case of sprue therapy, minimal doses of the steroids were found to be best. In the cases of Whipple's disease, ACTH has been found to be apparently more effective than cortisone in obtaining remissions. This is possibly because of the chemical molecular formula of these steroids. Cortisone has an 11-dehydro-17-hydroxycorticosteroid configuration,

and since there is an apparently greater action by the ACTH, there is the suggestion that this latter acts by stimulating the production of other corticosteroids than the 11-dehydro-17-hydroxy variety, possibly Kendall's Compound A, which is 11-dehydrocorticosterone. This Compound A has been found to increase the absorption of fat experimentally. Nothing else is known of any other beneficial effect of this particular compound.

*Dr. Sidney M. Fierst (Brooklyn, N. Y.):*—First, I want to thank the discussers for their great kindness. Secondly, I should like to say that only two names appear on the program as authors of this paper. Associated with us in this work were others whose names will appear on the published paper: Dr. Saul Feldman, Dr. Herbert Radack, and Dr. Abraham Langsam. Without them we probably could not have completed it.

A question has been asked as to the absorptive defects in hypermotility. There seems to be no significant decrease in the absorption of fat using chylomicron technic following the stimulation of peristaltic activity with prostigmine or neostigmine. I think, however, that would be a very fruitful subject for future research.

As to what effect motility has on the absorptive surface, it is possible that with hypermotility we get marked local segmentation and there will, therefore, be a greater lacteal surface area exposed to the food.

How can we diagnose these people before they come to the hospital? Well, the fact is, most of these patients come to the physician before they come to the hospital. There was one patient with a regional ileitis whose presenting complaint was that on several occasions she felt dizzy and almost fainted. In getting a further history, we noted a story of some diarrhea. The problem was explored further and regional ileitis was demonstrated. She was sent to a laboratory to have the blood calcium determined. The pathologist called in great dismay. He said that he had to rush out to a taxicab because the lady had a tetanic hypocalcemic convulsion in the taxicab. She had a blood calcium of 5—an atypical manifestation of steatorrhea.

We have had another patient who presented with a history of menorrhagia. She was actually admitted to the gynecological service for this symptom. The gynecologist examined her and could find nothing abnormal. The hematologist found her to have a prolonged prothrombin time. This led to the work-up that established the diagnosis of sprue. One must, therefore, be alert to the atypical manifestations.

# SINGLE LAYER END-TO-END INTESTINAL ANASTOMOSIS*

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The purpose of this communication is to present a series of 60 consecutive one layer intestinal anastomoses without leakage or death, and to discuss the experimental background, the technical considerations and the results.

In most hospitals today, intestinal anastomoses are performed in the traditional two layer manner sometimes with a continuous inner layer of chromic gut and an outer layer of interrupted nonabsorbable sutures or with interrupted sutures in both layers. These methods are used whenever an open anastomosis is performed, and open anastomoses have become increasingly popular since the introduction of antibiotics for intestinal antisepsis.

The ideal intestinal anastomosis is one in which there is exact approximation of the layers of the cut ends of the bowel without any cuff, without the use of sutures, with perfect continuity of the peritoneal covering and with immediate restoration of normal resistance to bursting, unaccompanied by morbidity or death. A single layer end-to-end union probably comes nearer to this ideal than any other. With it a very narrow cuff may be achieved with a minimum of suture material, and with minimal morbidity and mortality as demonstrated by this series.

## Experimental Background

Now let us consider the ideal intestinal anastomosis, as yet unattainable. Since the ends will not hold themselves together we must support them by sutures until such time as support is no longer needed. In all wound healing there is a short lag period after which strength increases rapidly.

When will healing tissue not only support itself but be able to resist the pressures within the intestine?

In 1887, Halsted[2] reported the results of his experiments on intestinal suture, pointed out the importance of the submucosal layer and demonstrated the adequacy of a one layer anastomosis performed with fine interrupted silk. Thirty-three years later, Sabin[6] made basic observations on the healing of end-to-end anastomoses and found that anastomotic blood vessels were present across the suture line within seven to nine days. In 1951, two studies were published which did give some answers.

Fellows et al[1] conceived the idea of testing the strength of an anastomosis without suture support and devised a method whereby the suture support

*Read before the Third Annual Convention of the American College of Gastroenterology, New York, N. Y., 15, 16, 17 October, 1956.

could be removed from the bowel at any time. Thus they were able to show that within 15 to 30 minutes after operation the peritoneal surface and ends of the united intestine were sealed by exudate which made the anastomosis air and water tight, but the resistance to inflation was negligible without suture support. With sutures the resistance amounted to 125 mm. of mercury using #60 cotton, or to 90 mm. of mercury using #000 chromic gut. At 24 hours the nonsupported anastomosis resisted a pressure of 50 mm. of Hg. and this continued the same during the lag period. On the fourth day the pressure resistance rose to 60 mm. of Hg. thence progressing to 165 mm., 245 mm. and 265 mm. of Hg. respectively on the fifth, sixth and seventh days. By the end of the third day sutured bowel withstood but 45 mm. to 65 mm. of Hg. intraluminal pressure. At this time the fibrin and suture strength were about equal. At the end of two weeks the anastomosis had approximately the bursting resistance of normal intestine, 400 mm. of Hg. or more.

From this study it is evident that suture support is required for at least four to five days, until the resistance reaches about 115 mm. to 150 mm. of Hg. With proper postoperative care, intraluminal pressures of greater magnitude are unlikely.

The studies were all made with one layer end-to-end anastomoses and when the specimens in animals were removed for testing, the inner surface of the anastomoses showed edema, necrosis and hemorrhage roughly proportional to the amount of trauma occasioned by the procedure. Healing appeared better when only the superficial layers of the bowel were sutured, without going through all layers but using the submucosa. Such an anastomosis produced almost no inversion cuff.

Sako and Wangensteen[7] applied these experimental findings to dogs and man, utilizing one layer end-to-end closed anastomoses. In essence they found that the width of the cuff was determined by the spacing of the sutures. With sutures 5 mm. apart a 5 mm. cuff was adequate. A smaller cuff could be obtained by placing the sutures from 1.5 mm. to 2 mm. apart without impairing the blood supply to the suture line. Their studies of the blood supply and blood vessel regeneration at the anastomotic site confirmed the earlier findings of Sabin, except that they did not find functioning communication of blood vessels until about 14 days.

## Clinical Material

The present series of 60 single layer end-to-end intestinal anastomoses were performed without subsequent leakage or death. Twenty-six were colocolostomies, 16 were enteroenterostomies of the small intestine and 18 were anastomoses of the small intestine to the colon. The distribution of cases is shown in Table I and the operations in Table II.

### Preparation of Bowel

All patients for elective resection involving the colon received 12,500 units of bacitracin and 125 mg. of neomycin orally every eight hours for the 48 hours before surgery. Thorough colonic irrigations and laxatives were employed in addition to the antibiotics, and constituted the more important part of preoperative preparation. Intake was restricted to fluids for 18 hours before operation. No preparation was used for small bowel resections. In many of the cases bacitracin and neomycin were given for three days after peristalsis had returned.

TABLE I

Location of Lesions

| | |
|---|---|
| Large Intestine | |
| Carcinoma of Right Colon | 14 |
| Carcinoma of Transverse Colon | 9 |
| Carcinoma of Left Colon | 21 |
| Diverticulitis of Left Colon | 2 |
| Small Intestine | |
| Intestinal Obstruction | 9 |
| Lymphosarcoma | 2 |
| Involved in Ca. of Colon | 3 |

Special attention should be paid to the thoroughness with which the colon is cleansed, as this is the part of preparation which often is neglected or performed haphazardly but which is so much more important than the administration of antibiotics.

TABLE II

Operations

| | |
|---|---|
| Colocolostomy | 26 |
| Enteroenterostomy | 16 |
| Enterocolostomy | 18 |

### Suture Materials

My preference is for #000 black silk although some surgeons like cotton or chromic gut. Probably #0000 silk or cotton may be sufficiently strong as indicated by Sako and Wangensteen[7]. Never should a size larger than #00 be used. The findings of Fellows et al[1] suggest that although #000 chromic gut may be used it does not offer quite the same degree of protection as cotton or silk. During the lag period the nonabsorbable suture is stronger and it is not subject to unforseen variation in rate of absorption. All sutures should be swaged onto atraumatic needles designed for intestinal use.

## Technic

One layer anastomoses may be performed closed or open as the situation demands. A closed method is better when bowel preparation is possible. Technically the use of fine Bainbridge clamps gives the surgeon excellent control over the bowel permitting accurate placement of sutures. The danger of suturing through both sides of the intestine may be avoided by penetration only as far as the submucosa.

The interrupted short mattress type of suture, with bites into the submucosa taken at right angles to the axis of the bowel and paralleling the cut ends, provides the narrowest cuff. Either interrupted Halsted mattress or Lembert sutures may be used but they result in somewhat wider cuffs. Interference with the blood supply is about the same. While a 5 mm. cuff is easily attained with sutures 5 mm. apart, a much smaller cuff is desirable and may be achieved by placing the sutures close together, about 2 mm. apart. There is less likelihood of necrosis with the Lembert as compared with Halsted or Dupuytren sutures.

A one layer open anastomosis may be performed but may be more difficult technically on account of the tendency of the mucosa to evert and the muscularis to retract and contract. Proper placement of three stay sutures makes for easier handling. This type of anastomosis has been used successfully in the area of the hollow of the sacrum during sphincter saving operations done by others. A suture should be placed in the center of the posterior row and then on each end. Thus the insertion of the remaining posterior sutures is facilitated. The same technic may be used on the anterior layer. Traction across a half section of bowel instead of the entire width gives better control and the mucosa is less troublesome. Also, the maneuver makes it easier to keep the suture line straight and the placement even.

When a side-to-side anastomosis is performed by the open method the posterior layer of sutures is placed, tied and cut and then the anterior layer is placed one centimeter from the posterior. The anterior sutures are retracted, half upward and half downward, to permit opening the bowel loops exactly between the two rows of sutures, thus creating a cuff of not more than 5 mm. End-to-side anastomoses are done in the same manner, either open or with clamps.

Regardless of the method used, an extremely important technical consideration is the proper tying of sutures. Care must be taken to bring about good approximation without strangulation of tissue. If knots are tied too tightly, particularly if mattress sutures are used, necrosis may follow.

Holman and Connolly[3], in 1952, restated Halsted's principles and technic and reported their modification of the aseptic anastomosis of Martzloff and Burget[5]. It consisted of withdrawing the two continuous Parker-Kerr catgut serosal sutures which the previous authors used to keep the bowel ends closed and which they allowed to remain in place after completing the anastomosis

with fine interrupted silk sutures. The modification is a good one and seems to produce a small cuff.

A telescopic cuff method of anastomosis using a single layer continuous suture was described by McCaughan[4], in March, 1955. He denuded the mucosal and muscular layers from one of the ends of the bowel and a corresponding amount of mucosa from the other. The two were fitted together telescopically and fixed in position by a continuous suture.

## Results

None of the anastomoses leaked. In one patient an obstruction developed distal to the anastomosis on the fifth postoperative day. Although much distention was present the anastomosis was found to be intact and healing nicely when the obstruction was relieved surgically on the sixth day.

Several patients had subsequent surgery for other conditions from six months to several years later. Their anastomotic sites were difficult to find and there were but minimal alterations of the bowel diameters.

Morbidity has not been increased nor have any of the patients died.

While most surgeons have become accustomed to performing two layer anastomoses, the technics described here are not difficult and result in anastomoses that are accurate and more nearly ideal without increasing morbidity or mortality. The secret lies in gentleness in tying knots, in handling tissues and placing small accurate bites so that the needle penetrates the submucosa.

One layer anastomoses are excellent in children, as the intestinal diameters are so small. Very fine sutures must be used. In 1954, Swenson[8] reported 32 children and infants in whom this procedure was employed. There were three deaths, none attributable to the anastomoses, as demonstrated by postmortem examination.

The telescopic cuff method of McCaughan resulted in considerable narrowing of the lumen of the bowel, which may have been due to the continuous suture or perhaps to redundancy of the mucosal cuff.

The interrupted suture methods described here have given very satisfactory results. Of the 60 cases reported, nine were subsequently examined by barium studies, one by sigmoidoscopy and eight during surgery for some other condition, making a total of 18. One patient had almost 50 per cent narrowing of the lumen of an ileotransverse colostomy, an incidence of about 5.5 per cent.

## REFERENCES

1. Fellows, N. M., Burge, J., Hatch, C. S. and Price, P. B.: Suture strength and healing strength of end-to-end intestinal anastomoses. S. Forum (1951), pp. 111-117, 1952.
2. Halsted, W. S.: Circular suture of the intestine: An experimental study. Am. J. M. Sc., **94**:436-461, 1887.
3. Holman, E. and Connolly, J. E.: Technical improvements in intestinal anastomoses. Stanford Med. Bull., **10**:196-202, (Aug.), 1952.

4. McCaughan, J. M.: Axial enteroenterostomy by a telescopic cuff method using a single row of continuous sutures: an experimental study. Surgery, **37**:446-454, (March), 1955.
5. Martzloff, K. H. and Burget, G. E.: Aseptic end-to-end anastomosis and a method for making closed intestinal loops suitable for physiologic studies. Arch. Surg., **23**:26, 1931.
6. Sabin, F. R.: Healing of end-to-end anastomosis with especial reference to regeneration of blood vessels. Bull. Johns Hopkins Hosp., **31**:289-300, 1920.
7. Sako, Y. and Wangensteen, O. H.: Experimental studies on gastrointestinal anastomoses. S. Forum (1951), pp. 117-123, 1952.
8. Swenson, O.: End-to-end aseptic intestinal anastomosis in infants and children. Surgery, **36**:192-197, (Aug.), 1954.

## Discussion

*Dr. Walter Shriner (Springfield, Ill.)*:—I think that this is probably the longest series of this type of anastomosis that has as yet been reported, and certainly it is one of the most exemplary.

As Dr. Beling says, we are coming closer to the ideal method and certainly it would be desirable if we could simply take the bowel and stick it together with some kind of glue, but our problem is that we do have a difficulty with leakage, pressure and the wound phenomena that occur in other places in the body also occur here. Certainly the technic is desirable. Personally, I prefer the #000 silk suture, applied by the Lembert procedure as advocated by Dr. Beling. I have used this mainly in the hollow of the sacrum.

I realize there is controversy regarding this situation. I think, certainly, the theory of Halsted, so many years ago, has not been applied within the realm of many of us here today. The period of intestinal distention, when the patient was in bed for two or three weeks with aerophagia and massive distention, made us all fearful of leakage. With reduced lumen pressure sealing is quick and we are less likely to get hemorrhage or leakage. Certainly the small anastomotic cuff is to be desired.

I must agree very strongly with Dr. Beling that unless we prepare the bowel adequately, we really should not attempt surgery except for obstruction. To my mind, castor oil is the only satisfactory solution to this problem. Frequently we have gone in and found "cement" in the bowel, the type of material spoken of by radiologists as barium, and with no bowel physiology at all established.

As to the speed with which air can be transported through the ileum, I have attempted to study this matter somewhat and have injected the Levin tube and noted how quickly air or gas will appear in the cecostomy opening and the speed with which the ileum functions. I think that has not been adequately understood until very recently nor was the problem of aerophagia. The transport speed of gas is often less than 30 minutes from stomach to cecum.

The old theory that ileus is primarily a traumatic thing must be abandoned.

There is a vast difference between sealing of the bowel and healing. If there is no pressure inside the bowel, obviously the bowel cannot leak, so I

have gone a step further by always introducing a large mushroom catheter proximal to the area of anastomosis. This has been frowned upon for the reason that too many times the bowel has not been adequately prepared and the catheter has become plugged up with feces or with barium cement, and therefore does not function properly. If this is proximal to the anastomosis, the air pressure within the bowel is obviously the same as the atmospheric pressure outside, and, therefore, much less tendency for leakage is present.

This is one step forward. Sooner or later, as Dr. Beling points out, he will have some complication, and probably the single-layer anastomosis technic will be unjustly blamed for it. If we continue with this method we will get at least one step closer to the ideal anastomosis.

I should like, also, to mention the vital importance of the four-day period in wound healing. We must realize that the strength of the healing wound is very minimal until the fourth day and then it rises with great rapidity. This cannot be done, however, if Vitamin C is absent or is in inadequate amounts. It is my custom to give at least 1,000 mg. of Vitamin C per day either orally or hypodermically, and, also, to supplement it by flavonoids to insure adequacy of the fibrotic process at the anastomotic cuff.

The avoidance of excessive interluminal pressuring during the four-day period would avoid the leakage problem through the recent seal. To this end I would urge consideration of the decompressive mushroom catheter.

Dr. Beling is to be congratulated on his lengthy series without any difficulty reported.

*Dr. Christopher A. Beling (Montclair, N. J.):*—I have just one very brief comment.

I was particularly interested to hear Dr. Shriner bring up the subject of postoperative care, because I think that the surgeon who performs in the isolation of the operating room, completely away from the gastroenterologist and internist, is rather sterile himself in his results. This whole field of gastroenterological surgery should be considered in terms of a cooperative enterprise. I think all of you would agree with that.

The surgeon can do a great deal technically, but the efforts of all of us may go to naught if the patient is not properly prepared, and certainly, if you don't care for him properly after the operation, a lot of the work is lost. There has to be good after care. Vitamins, fluids, blood volume replacement, replacement of electrolytes—they all play a role, and, if we forget them, the surgical results may not be good.

There was a time when speedy operations and big sutures were the order of the day. No longer are they in favor. Today we try to practice what I like to call informed surgery in a surrounding of cooperation among all branches.

# EVALUATION OF STANDARDIZED SENNA IN THE MANAGEMENT OF CONSTIPATION

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and

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The treatment of constipation is in essence as effective as the method has appeal to the patient.

The purpose of this study is to evaluate the effect of a newly standardized preparation of Cassia Acutifolia (Senna) pods* as the single method of treatment of functional constipation.

Our interest in this approach stemmed primarily from the prevailing indifference of patients to persist on a regimen that was designed to replete water, bulk and the manifold other approaches to functional bowel retention. Constipation is an abnormality which is easily tolerated, therefore, the treatment must be less unpleasant than the condition.

TABLE I

| Age Incidence | % | Duration | % |
|---|---|---|---|
| 16-25 years | 14 | 1 week-1 year | 12 |
| 25-50 years | 53 | 1-10 years | 68 |
| 50-83 years | 33 | 10-50 years | 20 |
| Total | 100 | Total | 100 |

A preparation which is convenient to transport, simple to take, as well as palatable, and one which is confined in its action to the colon, would have the greatest patient appeal and potential efficacy. It is on this basis that Senokot was selected for our study in the treatment of functional constipation.

This Senna preparation is standardized by chemical and biological assay[1] so that dosage and resultant action is controlled and predictable. One teaspoonful (3 gm.) is equivalent in activity to 450 mg. of the total activity of Cassia pods devoid of undesirable resinous matter which contributes to the so-called griping effect.

*The preparation used in this study is Senokot, supplied by the Purdue-Frederick Company.

The pharmacodynamics of Senokot are three active glycosides[2] which are absorbed in the upper small intestine via the blood stream and later reexcreted into the colon[3]. Activation by the bacterial flora permits release of the active principle which stimulates the parasympathetics by way of Auerbach's plexus resulting in physiological defecation[4,5]. This mechanism is in contradistinction to catharsis by bowel irritability.

It is not the intent of this discussion to delve into the multiplicity of etiology postulated as the genesis of uncomplicated constipation. Except for constipation resulting from stasis of a spastic colon, however, most constipation is acquired rectal and lower bowel hypasthesia. In other words, when the defecation reflex is deliberately and sufficiently ignored, atonic constipation is evolved. Therefore, restoration of a physiologically active colon with an end in view of eventual discontinuance of therapy when bowel tone has been restored is the desired effect from any regimen.

## Clinical Studies

Before administering Senokot to 122 patients, a brief survey was made as follows: No special age group was selected except that children were omitted

TABLE II

| Type of Constipation | % |
|---|---|
| Spastic | 18 |
| Atonic | 82 |
| Total | 100 |

from this study, since it was felt that parent influence rendered them less controlled subjects. Table I shows the age group and duration of constipation.

History, abdominal, rectal and sigmoidoscopic examinations were routine. Roentgenological studies were added when the diagnosis of functional constipation was in doubt. Seven per cent of our total cases surveyed demonstrated organic disease and were not included in this analysis.

Table II shows the types of constipation encountered.

## Method of Administration

In an attempt to evaluate objectively the efficacy of a standardized Senna preparation, each patient was advised to omit any previously prescribed medication, special diet, or method of inducing defecation.

The method of administering Senokot granules was constant, except in the cases of spastic constipation. In this group, it was anticipated that diarrhea

might follow too rapid an increase in dosage, and therefore, the maximum dosage was attained cautiously.

The schedule of dosage was as follows: An initial dose of one teaspoonful of the granules was given nightly according to the patient's preference in fluids or swallowed without dilution. If normal defecation did not follow after two days, the dosage was increased by one-half teaspoonful. The maximum dosage established was two teaspoonsful twice daily.

After regularity persisted for four weeks, the dosage was reduced to the smallest maintenance possible, and later omitted when advisable.

## Results

Our original supposition of simplicity and palatability of medication met with universal favor.

TABLE III

| Dosage Requirements | % |
|---|---|
| Less than ʒi | 5 |
| ʒi | 33 |
| ʒiss | 28 |
| ʒii | 20 |
| ʒiii-ʒiv | 14 |
| Total | 100 |

Secondly, the time of evacuation stabilized itself in the majority of instances, to the first hour or two after awakening. This seems to be consistent with the fact that about eight hours is required from the time of administration to that of stimulation of the myoneural junction of the colon.

Interrogation as to the character of the stool invariably elicited a transition to a physiologically normal consistency.

As will be noted in Table III, 38 per cent of the patients attained regularity of defecation with a dosage of not more than one teaspoonful every evening at bedtime. Forty-eight per cent of the patients required over one teaspoonful, but not more than two teaspoonsful, and only 14 per cent of this series required three teaspoonsful or a maximum of four teaspoonsful. The latter was given in divided doses twice daily. Of this group, it was found that the dosage could be reduced after three or four weeks to a maintenance dosage of one to two teaspoonsful daily.

In the spastic constipation group, the maximum dosage was abruptly dropped to an average of one teaspoonful nightly as soon as the initial bout of bowel retention was obviated. There was less evidence of abdominal cramps on this regimen than was noted previously with other anthracene cathartics. This manifested itself primarily during the initial phase of dosage, and was not complained of when dosage was adjusted.

## Conclusions

Cassia Acutifolia (Senna) pods (Senokot) is a simple, palatable, easily-administered constipation corrective. The dosage is flexible, yet within the scope of physiological tolerance.

It has been our observation that patient appeal to the preparation has made this study more exacting inasmuch as the method and period of administration was for the most part followed to the letter.

The side-effects consisted of occasional episodes of transitory diarrhea until dosage was individualized. Abdominal cramps were complained of in seven per cent, which represented particularly the spastic constipation group, until the minimum effective dosage was reached.

Ninety-five per cent of the total could be satisfactorily regulated, whereas the remaining five per cent were unable to be adjusted on dosage that would produce a normal type of dejection consistent with the criterion for this study because of aberration of physiology of the colon.

## Addendum

Melanosis coli has been experienced with some anthracene derivatives. No evidence of melanosis coli has been observed in this series of cases. A longer follow-up is intended and will be reported on at a later date.

## REFERENCES

1. Lou, T. C.: Pharm. Pharmacol. **1**:673, 1949.
2. Fairbairn, J. W. and Saleh, M. R. I.: Pharm. Pharmacol. **3**:918, 1951.
3. Gaddum, G. H.: Pharmacology, page 251, 4th Edition, Oxford Press, London, 1953.
4. Abrahams, Sir Adolphe: British Encyclopedia of Medical Practice, Interim Supplement, March 1954.
5. Straub, W. and Triendl, E.: Archive fur Experimentelle Pathologie und Pharmakologie, **185**:1-19, 1937.

# A PRESENT DAY SURVEY OF FLEXIBLE TUBE ESOPHAGOSCOPY*

EDWIN BOROS, M.D., F.A.C.G.

New York, N. Y.

This discourse proposes a clarification and appraisal of flexible tube esophagoscopy since its introduction by the author in the year 1947[1]. Much progress has ensued since; if not in the actual detailed performance of the original concept and method, at least in the application or development of subsequent instruments all of which embrace in part the basic facts and principles pointed out by the speaker in his original presentation[2]. One cannot fully and properly present this subject in its suitable setting without its appropriate background of centuries of restrained and retarded development which nature, by anatomy and physiology, had contrived and which the physician in his limitations has accorded in. It is not surprising therefore, that were one to gauge and appraise the sum total knowledge of the esophagus in terms of pages and chapters, it will be found that by comparison with other organs of the digestive tract it appears in a somewhat reduced state at the present time. It can be pictured as being in the twilight zone of development.

Instrumental exploration of the gullet by means of the flexible esophagoscope has afforded an opportunity of conducting observations and studies of this organ in patients complaining of the ubiquitous symptom of heartburn[3]. These studies have been published and are probably known to many of you. I am certain that by no means prior to 1947 could such a venture have been performed. Neither patient, clinician nor one's conscience would have permitted it. In the beginning, when fancy and fantasy unfolded boundless horizons of exploration and research, every opportunity for instrumentation was sought for, far too often with those disappointments so well known to all adventurers. Numbered amongst patients who were subjected to this procedure was one who comes to mind so vividly—a victim of leukemia. This subject revealed on esophagoscopic examination a hitherto unobserved and unknown phenomenon—at least to the speaker—the presence of an elevated circular mound of purplish hue, resembling a hematoma—in reality a leukemic tumor of the posterior wall of the esophagus just below the cricopharyngeus muscle.

Strange views of esophageal varices have likewise been seen from time to time, nothing like the beautiful pictures so neatly described in textbooks. It might be mentioned we don't hesitate to pass a flexible tube in a patient suspected of varices, except where there is active bleeding. One does not at all times see the distended worm-like elevations so characteristic of this disorder. A marked mucosal edema and congestion sufficiently advanced on occasion to

*Read before the Annual Convention of the American Gastroscopic Society, Chicago, Ill., 10 June 1956.

cause an apposition of the walls, with nothing but intense engorgement and friability has at times been observed. The enlarged veins are apparently buried in the swollen mucosa. A few patients with jaundice have likewise been esophagoscoped. It has been stated that for the detection of border line cases of jaundice, the frenulum under the tongue displays early discoloration not otherwise detectable on the skin. Jaundice is well characterized by a markedly intense discoloration of the esophageal mucosa—somewhat more distinctive than that of the integument itself. While portal cirrhosis is frequently associated with dilated esophageal veins, one must not underestimate other possible causes of this affection. A small but distinct vein recently viewed in the mid portion of the gullet may be the only positive finding in a patient with melena. The finding is at least a signpost if not an actual assurance of true direction. Further, the symptom of heartburn whose status cannot be labelled, merits visual inspection of the swallowing tube. Only in this way is it possible to avoid some of the strictures which occur in this region.

These are but a few examples illustrating how observations in this fertile field may well crystallize into knowledge, and as new channels of study open up, undreamed of effects cannot help but follow. The mechanism by which these examinations have been conducted needs no revision. The procedure has been described in great detail and it would be trite to belabor it. Uncertainties, problems, some timidity, are all natural expectations in all new methods of fields of endeavor. It might be appropriate at this time to clarify some of these that have been brought to my attention. Schindler's attainment of a practical flexible gastroscope was the culmination of prior effort to gain entrance to and explore the gastric cavity. By comparison, however, there was no such movement, nor was there any thought of the need for improvement in instrumentation of the esophagus with rigid tubes, despite its dangers and shortcomings. It was accepted with equanimity. It is no wonder that the gastroenterologist's knowledge of this area kept pace with the limited interest and scope of the laryngologist in whose hands this instrumentation reposed. Under the circumstances it could not be otherwise. It was purely a matter of mechanics. There lay the roadblock to progress. As a matter of interest, the author has had a thorough training over many years in the use of rigid tubes, and in modesty, had no worse experience than those of his confrères. The flexible tube was evolved therefore with a background and knowledge of the problems of the day, which incidentally included first hand information of the various instruments then in use. Included in these, there was a direct replica of one that is being advertised widely today. It consisted then, as it does now, basically, of a rigid tube within which there was and is contained a removable flexible obturator. It concerned itself merely with the problem of introduction and left the operator then, as it does now, "on his own" during the remainder of the examination. In effect then, after passage through the oral cavity one is actually working with a rigid instrument. But by

no means is it implied that this circumstance makes this a bad instrument. It may well serve the purpose of the user who may be quite happy with it, just as I was with rigid tubes. The concept of flexible tube esophagoscopy is, however, quite different. There is no ambiguity about it. It means what it says. Complete flexibility throughout and *during the entire examination, not only during passage through the pharynx.* The safety factor resides in this important feature and envisages extraneous encroachments on the lumen as well as encumbrances within, and lastly and most important, the anatomy of the lower esophagus is not disdained. A problem all its own is confronted here, because there takes place an unmistakable veering of this organ anteriorly and to the left, and if one is to negotiate this turn safely and not pay the price of past misfortunes, extreme caution and a light touch, if ever required, finds its need here. The value of a soft tip in this region requires no emphasis.

Inasmuch as so many gastroscopists have now become esophagoscopists as well, it might be pertinent to advance a few thoughts on the difference in the basic mechanics of both these procedures. The former presupposes the existence of an open lumen and clear field before attempted instrumentation is effected. Exploring the esophagus in the face of obstruction from within or extraneously is an *invitation* rather than contraindication for esophagoscopic procedure. Gastroscopy performed blindly is proper practice, provided the usual safeguards are enforced. Actual and intimate visual observation is at all times an indispensable condition in the performance of an esophagoscopy as soon as the organ is entered and clear vision is afforded.

All that has been said will have lost force if certain fundamental features are not carried out prior to instrumentation. Adherence to detailed preliminary preparations cannot be dispensed. A little effort here can avoid peevishness to both patient and performer. A frisky patient is a bad one for passing instruments. Demerol intravenously in doses of 50 to 100 mg. have been oft resorted to favor complacence in a patient who had already been medicated with the routine hypodermic intake of 3 grains of sodium luminal followed by the usual quarter grain morphine and one one-hundredth grain atropine sulfate. Our emphasis on the so-called sermon to the patient is a ritual in our technic. With the patient fully aware as to the nature of the procedure, his acquiescence and cooperation are assured for the completion of a simple and safe technic. The performance can no more be done satisfactorily otherwise, than it would be possible to hypnotize a subject against his will. It has seldom been necessary to use a general anesthetic during the introduction of a flexible esophagoscope. Such is not the case when employing rigid tubes. Efforts obviously are directed towards simplification of the procedure to its limit. The addition of a general anesthetic does not do this. Adding difficulties to the performance will not invite future referrals, defeats the basic theories, and is in conflict with proved experiences which have become a reality.

It was not so long ago that the average physician or surgeon would shrink when confronted by the thought of esophagoscopic instrumentation, and in no small measure has such an attitude in the past been justified. Nor has the patient himself shared a different feeling in the past. And so, if we are to make progress which good leadership and combined cooperation permits, we must be attuned, we must be ready to accept the newer developments which some of us at times are a little hesitant to accept, and if we are to investigate and evaluate and add further to our resources, we have the means by which we can do so. It has been asked how intense is the actual need for instrumental esophageal exploration? Can it be performed routinely? The answer depends on what one has in mind. If one desires to investigate, complete freedom and safety is assured with ease to the patient. Where one wishes to treat, facility of manipulation is afforded. For more concerted and expansive surgical endeavor, the operator is spared the ordeal and danger of past experiences.

## REFERENCES

1. Boros, Edwin: Esophagoscopy By Means Of A Flexible Instrument. A New Esophago-Gastroscope. Gastroenterology. **8**:724-728, (June), 1947.
2. Boros, Edwin: Flexible Tube Esophagoscopy. Gastroenterology. **11**:879-882, (Dec.), 1948.
3. Boros, Edwin: Relationship Of The Esophagus To Heartburn. Rev. Gastroenterol. **2**:132-137, (Feb.), 1953.

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## *President's Message*

### Vice Presidents at Work

An organization is only as effective as the teamwork of its officers and committees. In keeping with this concept, the President-elect and each Vice President is given an opportunity to observe the functions of assigned committees each year as he ascends the ladder to the Presidency.

In being assigned to committees, he must observe them; give advice when requested; help in their functions if such help is needed; seek advice from higher echelons if necessary and assume the responsibility and see to it that the chairmen do their jobs well.

This is how it works: As 4th Vice President he is assigned to the Public Relations, Editorial and Publications, and Nominating Committees.

As 3rd Vice President he is assigned to the Program, Convention Arrangements, Postgraduate Education, and Regional Meetings Committees.

As 2nd Vice President he is assigned to the Finance, Research, and Endowment Fund Committees.

As 1st Vice President he is assigned to the Credentials, Revision of Constitution and By-laws, and Hospital Relationships Committees.

As President-elect, he is chairman of the Membership Committee. He is also assigned to work with the Secretary, Secretary-General, Treasurer, and the Executive Director.

All Vice Presidents are on the Membership Committee each year until they assume its Chairmanship as President-elect.

Under this scheme of assignments it is obvious that when the 4th Vice President becomes President, he will have a most thorough understanding of our College and will, therefore, be prepared to serve well.

Arthur A. Kirchner

## NEWS NOTES

### American Gastroscopic Society

The Annual Meeting of the American Gastroscopic Society will be held at The Broadmoor, Colorado Springs, Colo., Thursday, 16 May 1957.

The program will consist of a series of individual papers and a panel discussion on "The Evaluation of Clinical Methods for Examining the Esophagus". Participating in the panel will be Drs. Joseph Kirsner, Samuel D. Kushlan, Frank B. McGlone, Frederick Templeton, Moses Paulson and Edward B. Benedict.

Further information and a complete program may be obtained from the Secretary-Treasurer, Dr. C. Wilmer Wirts, 1025 Walnut St., Philadelphia 7, Pa.

### American Board of Internal Medicine

Oral examination for candidates on the West Coast will be given in Los Angeles, Calif., 11-14 September 1957.

Further information may be obtained from Dr. William A. Werrell, Executive Secretary-Treasurer, The American Board of Internal Medicine, 1 West Main St., Madison 3, Wisc.

### Fellowship Keys

Keys for *Fellows* of the American College of Gastroenterology have been authorized by the Board of Trustees. An illustration of the key is at the left.

These may be ordered from the headquarters office, 33 West 60th Street, New York 23, N. Y., at $10.00 each including federal tax and shipping charges.

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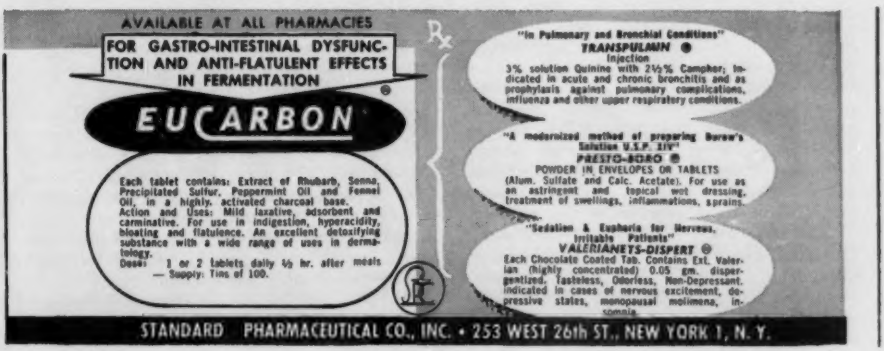
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## GASTROINTESTINAL TRACT

### THE DIFFICULT DUODENAL STUMP: Clarence E. Sanford. U. S. Armed Forces M. J., 7:336 (Mar.), 1956.

Successful management of the difficult duodenal stump requires a thorough knowledge of the distorted anatomic structures in the region and a recognition of the pitfalls of overzealous dissection. A good watertight closure, adequately covered, decompression of the afferent limb of the gastrojejunostomy, and maintenance of an adequate blood supply are of paramount importance. Catheter duodenostomy is a safe alternative to precarious closure and, when the tissues of the duodenal stump defy any other type of handling, provides a sound method of dealing with the difficult duodenal stump.

ARNOLD L. BERGER

### CORRELATION OF GROSS GASTROSCOPIC FINDINGS WITH GASTROSCOPIC BIOPSY IN GASTRITIS: Leonard Atkins and Edward B. Benedict. New England J. Med., 254:641 (5 Apr.), 1956.

The authors state, that since the development of the flexible operating gastroscope and the addition of the flexible gastric-biopsy tube our interest in the gastritis problem was greatly stimulated. Our attitude to normalcy and to pathology had to be revised. During the period from March 1946-June 1954 the authors performed 401 gastroscopic examinations, did 391 biopsies, 258 of them concerning the problem of gastritis. 239 of the latter ones were tabulated and analyzed showing a striking discrepancy between gastroscopic impressions and histological findings. The authors state that especially the verrucous appearance of the gastric mucosa – formerly thought of as pathognomonic for hypertrophic gastritis–represents in most of the cases a normal histological picture. Therefore hypertrophic gastritis should be abandoned as a pathological entity. Furthermore the "reddening of the mucosa" seen in so-called acute gastritis histologically very often does not represent true acute gastritis. In conclusion the authors postulate that any form of gastritis should be diagnosed only after gastroscopic biopsy.

HANS J. JOSEPH

## ESOPHAGUS

**STRICTURE OF ESOPHAGUS DUE TO ACCIDENTAL INGESTION OF URINE TESTING TABLET: Marvin I. Lasky and H. N. Picard. Illinois M. J., 109:30 (Jan.), 1956.**

A case history is presented of esophageal stricture in the midesophagus caused by the accidental swallowing of a Clinitest tablet. The stricture occurred despite immediate use of antidotes (vinegar) and treatment by the family physician. Esophagoscopy revealed a 6 mm. wide stricture which was treated by passing metal bougies over a previously swallowed silk thread with complete functional recovery. The first symptoms occurred approximately two weeks after the accident and became progressively worse until at the time of treatment six weeks later she could not swallow fluids.

STANLEY STARK

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**ESOPHAGEAL ATRESIA WITH TRACHEO-ESOPHAGEAL FISTULA: John W. Donald and James G. Donald. J.M.A. Alabama, 25:201 (Mar.), 1956.**

The authors have encountered three patients with the above condition during the past five years. All three had the same anatomic type of anomaly, namely, the proximal esophageal segment ended in a blind pouch and the distal segment communicated with the trachea. In the first case a retropleural approach to the esophagus was used whereas in the last two cases a transpleural approach, as advocated by Koop, was used. The latter is felt to be far superior, allowing better exposure and less chance of an anastomotic leak. The authors feel that, with proper anesthesia, these infants tolerate the open pleural cavity quite well. Gastrostomy was performed in all three cases and the authors felt it contributed to the successful results. Spontaneous closure usually occurs following removal of the gastrostomy tube and a secondary operative closure is not necessary. Early diagnosis and prompt treatment of this condition, which is most often seen in premature and small babies, is emphasized.

JOHN J. MCMAHON

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**FREQUENCY OF THE ASYMPTOMATIC LOWER ESOPHAGEAL CONTRACTILE RING: Philip Kramer. New England J. Med., 254:692 (12 Apr.), 1956.**

The author reviews 100 patients by means of fluoroscopy and radiography of the esophagus. Unfortunately these patients are not "normals" but are patients with complaints referable to the gastrointestinal tract unrelated to the esophagus. In six of these the author discovers a contractile ring in the area of the phrenic ampulla. He suggests that the frequency of an asymptomatic contractile ring, six per cent of his series, is higher than that previously reported, one to two per cent. This, however, is a selected series as he notes. He concludes that before such a contractile ring is accepted as the cause of dysphagia a patient should be submitted to a barium food or barium capsule test to observe whether or not the ring is actually causing an impedence to the passage of material through the esophagus.

This paper presents a lesser known syndrome, that of esophageal ring, and emphasizes the necessity for applying a simple method of diagnosis—the barium food or barium capsule test.

RALPH D. EICHHORN

## STOMACH

**APPLICATION OF A DIET TO GASTRECTOMIZED PATIENTS: R. Soupault and G. Pequignot. Arch. Mal. de l'App. Dig., 44:1249, 1955.**

Actual tolerance and ingestion were studied in the immediate postoperative period in 91 patients who had undergone operations on the stomach (excluding total gastrectomy) in relation to the application of a progressive realimentation diet in four stages. This diet, of which the details are given, involved the systematic use of milk.

1. A sufficient ration for the probable balance in nitrogenous matter (60 gm. of proteins and 500 calories) is exceeded on the 8th day after the operation in 85 per cent of cases; between the 9th and 12th days in all other cases except one, and on the 16th day in one case. A sufficient ration for the probable positive balance in nitrogenous matter (80 gm. of protein and 2,000 calories) was exceeded on the 9th or 10th day in 78 per cent of cases (and 75 per cent of the gastrectomies) and on the 12th or 13th day in 90 per cent of the cases.

2. Tolerance is good; in particular (except after Dragstedt's operation), diarrhea is relatively rare (if one does not count the 24 hours immediately following): 6 cases out of 65 gastrectomized patients. In four out of six of these cases milk does not seem to be responsible.

After Dragstedt's operation, diarrhea was observed in 4 out of 6 cases.

3. The correlation between the ration offered and the amount actually consumed is good. Actually, the fourth stage of realimentation (more than 80 gm. of protein and more than 2,000 calories) cannot be reached before the fourth day of realimentation. This is reached in 4-6 days in almost all patients who have been realimented on the 4th or 5th day following operations.

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**THE DIFFICULT DUODENAL STUMP: C. E. Sanford. U. S. Armed Forces M. J., 7:336 (Mar.), 1956.**

Successful management of the difficult duodenal stump requires a thorough knowledge of the distorted anatomic structures in the region and a recognition of the pitfalls of overzealous dissection. The accepted theories for duodenal stump leakage are reviewed and each is discussed as it pertains to the problem; these are: 1. obstruction in the afferent limb of the gastrojejunostomy; 2. inadequate blood supply to the duodenal stump; 3. precarious closure of the duodenal stump; 4. digestion at the suture line of closure of the duodenal stump; and 5. systemic factors affecting healing of the duodenal stump.

Of paramount importance are a good watertight closure, adequately covered, decompression of the afferent limb of the gastrojejunostomy, and maintenance of an adequate blood supply. Catheter duodenostomy is a safe alternative to precarious closure and, when the tissues of the duodenal stump defy any other type of handling, provides a sound method of dealing with the difficult duodenal stump.

ARNOLD L. BERGER

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## LIVER AND BILIARY TRACT

**EVALUATION OF ORAL CHOLECYSTOGRAPHY IN LIVER DISEASE: William Mandel, L. M. Gaines, Jr. and R. J. Marilley, Jr. A.M.A. Arch. Int. 97:335 (March), 1956.**

In an attempt to improve the differential diagnosis between intra- and extrahepatic biliary diseases, 40 patients with various liver diseases were given various liver function tests as well as oral cholecystography. Six tablets of Telepaque were administered for the latter procedure but somewhat better results were obtained with 12 tablets. The serum bilirubin level and the B.S.P. retention correlated best of all liver function tests with the gallbladder visualization. There were no untoward effects from the bromosulfophthalein or the Telepaque in any person with liver or galbladder disease. It was found that a normal gallbladder should visualize in any hepatic disorder with less than 20 per cent B.S.P. retention 45 minutes after intravenous injection of 5 mg. per kg. of the dye or with the bilirubin level of less than 5 mg. per 100 c.c. Absence of a gallbladder shadow under these circumstances meant either primary extrahepatic or associated extrahepatic biliary disease. Intravenous cholecystography with Cholografin should yield a greater incidence of gallbladder visualization in patients with liver diseases. There are no contraindications for this procedure in patients with liver diseases with or without jaundice. However, no investigation has been done with the latter procedure.

H. B. EISENSTADT

**BILIARY TRACT STUDIES. I. X-RAY DIFFRACTION ANALYSIS OF GALLSTONES; CORRELATION WITH OCCURRENCE OF MICROSPHEROLITHS IN BILE: Kerrison Juniper, Jr. and William E. Woolf. Am. J. Med. 20:383 (March), 1956.**

Most gallstones consist of very small particles, so-called microliths, representing the nuclei of stone formation. Microliths are either aggregates of cholesterol crystals, amorphous calcium bilirubinate granules or microspheroliths. The latter are organized crystalline structures and can be investigated like mineral with x-ray diffraction, a method analyzing the structure of crystalline compounds by passing an x-ray beam through it and recording deviation of these rays on photographic film. This investigation disclosed that microspheroliths are composed of calcium carbonate in the form of vaterite, aragonite and calcite. In addition calcium oxalate and phosphate were occasionally found. Milk of calcium bile contained mostly calcium carbonate while the wall of the porcelain gallbladder consisted of calcium phosphate.

Microspheroliths can be seen microscopically in the bile after duodenal drainage as colorless, grey or green crystalline structures having the shape of cubes, dumbbells, lemons, spheres, ovoids, wheat sheaves, clubs or stars. Such finding suggests a tendency to gallstone formation or actual presence of stones.

H. B. Eisenstadt

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## PATHOLOGY AND LABORATORY RESEARCH

**EVALUATION OF A RAPID SERUM AMYLASE TEST: Michel Gilbert. J.A.M.A. 158:775 (22 Oct.), 1955.**

Using the rapid serum amylase test described by Fishman and Doubilet on cases exhibiting upper abdominal pain seen in an emergency room service, the author found an accuracy for the test of 94 per cent compared with simultaneous studies made with the Somogyi test. After discovering the need for fresh starch solution (not older than three weeks) and proper changing of the iodine reagent the test used in the last 24 consecutive determinations has been 100 per cent correct.

The values of the test in addition to accuracy are the easily obtainable materials, rapidity of obtaining results (5 minutes after blood has clotted) and the minute amounts of serum required (0.1 c.c. and 0.05 c.c.). Also the end points are clear and easily interpreted.

W. K. Billingsley, Jr.

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**SERUM AMYLASE AND ACUTE ABDOMINAL DISEASE: W. Burnett and T. D. Ness. Brit. M. J. 4942:770 (24 Sept.), 1955.**

Serum amylase was estimated in a consecutive series of 350 patients admitted to the hospital with acute abdominal pains. There were 12 cases of acute pancreatitis. The amylase levels in these 12 cases varied from 1,200 to 6,000 Somogyi units. Determinations were made within 24 hours of admission, before operation or administration of morphine sulfate. It has been pointed out that morphine sulfate in the presence of an actively secreting pancreas can cause significant elevation in the level of serum amylase. This may be due to spasm of the sphincter of Oddi. A control series of 50 estimations in normals gave a range of 62-177 Somogyi units. The standard deviation was 33. Since very little apparatus is required this test was found to be adaptable for ward-side room work.

This test while useful in differential diagnosis is not absolutely pathognomonic. Values over 400 units were found in eight cases of perforated peptic ulcer. The highest being 3,400 units, found in a case of ruptured gastric ulcer seven hours old with 800 c.c. of fluid in lesser sac. The high values in these cases are due to the absorption of the spilled duodenal contents so that the levels depend on the duration of perforation and the amount of contamination.

Two cases of intestinal obstruction gave values of 1,600 to 2,000 units respectively.

Here the high values were probably due to increased absorption of intestinal amylase through capillaries and lymphatics in a damaged bowel wall.

In 12 of 23 cases of acute cholecystitis the serum amylase was elevated but in only two were the values 500 units. The serum amylase can be of real help in the differential diagnosis of this condition.

Moderate elevations, the highest being 800 units, were found in 57 cases of appendicitis. These increased levels in acute appendicitis may be due to increased activity of amylase producing organisms in the lumen, and increased absorption. Many other similar cases had minor values. Minor elevations occurred in a number of varied conditions such as in 10 of 15 urinary tract infections, none of which had symptoms of renal failure, a case of Meckel's diverticulitis and in abdominal carcinomatosis from carcinoma of the cecum. No increase was found in six cases of diverticulitis.

ALEXANDER ZABIN

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**OBSERVATIONS ON EPITHELIAL CELLS EXFOLIATED FROM THE UPPER GASTROINTESTINAL TRACT OF PATIENTS WITH PERNICIOUS ANEMIA, SIMPLE ACHLORHYDRIA, AND CARCINOMA OF THE ESOPHAGUS AND STOMACH: Barbara W. Massey and Melvin I. Klayman. Am. J. M. Sc. 230:506-514 (Nov.), 1955.**

These studies on epithelial cells exfoliated from the upper gastrointestinal tract were done on patients with pernicious anemia in relapse and in remission. The squamous cells were found to show multinucleation, atypical chromatin pattern and an increase in the cell size in 30 per cent or more of the exfoliated cells. The squamous cells return to normal during a remission or following adequate therapy. The columnar cells show characteristic changes during a relapse. However, unlike the squamous cells, large so-called "bland" columnar cells do not change even during a remission or after therapy. The presence of these cells is usually associated with severe gastric atrophy. Some so-called "active" columnar cells are found which are difficult to distinguish from malignant cells.

The authors concluded that a pernicious anemia relapse presents a cytologic picture of enlarged atypical squamous and columnar cells which is characteristic of the disease but not necessarily specific. After therapy, the squamous cells return to normal but the columnar do not. The so-called "active" columnar cells seen occasionally in pernicious anemia were also found in some cases of carcinoma of the stomach. The columnar changes reflect a permanent change. The active columnar cells have not been found in simple achlorhydria or nonpernicious anemia patients except when gastric carcinoma was present. It is suggested that patients with active columnar cells be carefully studied to determine a possible relationship of these cells to carcinoma.

BERNARD FARFEL

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**ELECTROPHORETIC STUDIES OF THE LIVER COMPONENTS IN SURGICAL DISEASES OF THE UPPER ABDOMEN: Toshio Sato. Tohoku J. Exper. Med. 62:315 (25 Nov.), 1955.**

Fraction P of liver components was studied both by electrophoretic and actual weighing methods, and the C fraction computed as the difference between the P fraction value and 100.

P protein value in gastric ulcer varied between 88 and 61 per cent, while in gastric cancer the variation was between 93 and 54 per cent, but values below 70 per cent occurred in but 3 cases of 34 in the gastric ulcer group, while values below 70 per cent occurred in 14 out of 54 gastric carcinoma cases.

Careful weighing indicated that a P protein value of 80 per cent corresponds to a liver protein value of 13.0 d/gl by electrophoretic method of study.

Operations for upper gastric pathology will cause a drop in P protein values, except where 500 or more c.c. of transfused blood is used during operation.

In cases of frank liver disease the P protein values were constantly low.

J. EDWARD BROWN

**STUDIES ON THE LABILE LIVER PROTEINS IN SURGICAL DISEASES OF THE UPPER ABDOMEN: Toshio Sato, Ko Segawa, Yasuo Kumei, Seiki So, Tsuneo Ando and Eiichi Naganuma. Tohoku J. Exper. Med. 62:303 (25 Nov.), 1955.**

Electrophoretic studies of labile "liver protein" show values of from 12.9 to 17.95 d/gl in the United States, but in Japan values of 12 to 14 d/gl are found in gastric ulcer, gastric carcinoma and chronic gastritis. Values falling below 13.0 d/gl were observed in advanced ulcerous and cancerous conditions where complications were present, and values below 9.0 d/gl were constant where operation was contraindicated.

In cases under operation the tendency of the protein to decrease was constant, but within 2.0 d/gl. Where 500 c.c. of transfused blood was used the decrease was less than 1.0 d/gl.

Specimens from the right or left lobe of the liver showed a variation of less than 0.5 d/gl, but in absence of transfusion the right lobe protein fell 1.1 d/gl to 2.0 d/gl lower than the left lobe protein.

Further studies indicated that liver disease, (experimentally produced by subcutaneous chloroform injections in healthy animals), decreases markedly the labile "liver protein".

J. Edward Brown

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**THE EFFECTS OF RESERPINE AND CHLORPROMAZINE ON GASTRIC SECRETION: Bernard J. Haverback, Thomas D. Stevenson, Albert Sjoerdsma and Luther L. Terry. Am. J. M. Sc. 230:601-604 (Dec.), 1955.**

The authors were moved to make this study because abdominal cramps and diarrhea have been noted during the administration of reserpine. Constipation has been noted following the use of chlorpromazine. Since these effects suggest action involving the gastrointestinal tract, studies on gastric secretion were done. Reserpine was shown to increase the volume and the free acidity of gastric secretion. Chlorpromazine was shown to decrease the volume of gastric secretion without changing the free acidity. The authors suggest that chlorpromazine would be the agent of choice where the sedative action is desired. It would appear that reserpine should be given with caution where there is a history or suspicion of peptic ulcer. It is believed that reserpine stimulates the motor function of the gastrointestinal tract leading to abdominal cramps and diarrhea. Gastric secretion is probably increased by reserpine because of the stimulation of the parasympathetic ganglia. The mechanism by which chlorpromazine decreases gastric secretion has not been found.

Bernard Farfel

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**BLOOD VOLUME IN PATIENTS WITH LAENNEC'S CIRRHOSIS OF THE LIVER AS DETERMINED BY RADIOACTIVE CHROMIUM TAGGED RED CELLS: S. Eisenberg. Am. J. Med. 20:189 (Feb.), 1956.**

Eisenberg studied the blood volume red cell mass and plasma volume in 20 patients with Laennec's cirrhosis of the liver by the radiochromium labeled "Red Cell Technic". A significant increase in plasma volume was noted only in patients with esophageal varices and/or cyanosis. In the absence of these features all of the measured functions were normal. The plasma volume and red cell mass were increased in four cirrhotic subjects with cyanosis. There was no true anemia nor was there a significant rise in red cell mass following clinical improvement. No consistent changes in plasma volume followed the recession of ascites. One patient was studied prior to and following the establishment of a portacaval shunt. In addition to esophageal varices, this patient exhibited striking collateral vascular channels on the abdominal wall. Following the shunt procedure, all evidence of collateral circulation disappeared and there was a concomitant decrease in plasma volume.

John M. McMahon

# BOOK REVIEWS FOR GASTROENTEROLOGISTS

**THE BILIARY TRACT: WITH SPECIAL REFERENCE TO THE COMMON BILE DUCT: Julian A. Sterling, A.B., M.D., Sc.D., F.A.C.S., F.A.C.G. 424 pages with numerous illustrations. The Williams & Wilkins Co., Baltimore, Md., 1955. Price $10.00.**

This is a well written and illustrated book dealing with the biliary tract, especially the common bile duct and the pancreas. Dr. Sterling has done a great deal of work on the biliary duct, and is well grounded in the subject. He has written many articles and several years ago, was the winner of the essay contest sponsored by the National Gastroenterological Association.

The text is divided into fifteen parts, each one of which is complete and well written. The illustrations are excellent and the colors are well reproduced. Diagnosis, including laboratory observations, radiology, medical and surgical management, pre- and postoperative conditions, are discussed. An extensive bibliography and an adequate index add to the value of the book.

Dr. Sterling and the publishers are to be commended for bringing out this beautiful volume. The reviewer recommends it with pleasure as a valuable adjunct to the library of all physicians.

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**LEHRBUCH DER VERDAUUNGSKRANKHEITEN (Textbook on Digestive Diseases): Prof. Dr. N. Henning, Director of the Medical Clinic, University Erlangen and Doz. Dr. W. Baumann, Drector of Roentgenology, Bethel/Bielefeld. 562 pages, 335 black and white illustrations. Second revised edition. George Thieme, Stuttgart, 1956. Price $18.35.**

Before World War II, the reviewer had the pleasure of meeting Dr. Henning and observing his work. Although still a young man, his observations, deductions and gastroscopic technic added a great deal to our present knowledge in the gastrointestinal field. In this second revised edition of his text on gastroenterology, Dr. Henning's collaborators, Dr. Hans Kirzlmeier, Dr. Ludwig Deruling and Dr. Klaus Heinkel, added new and important material dealing with the stomach, biliary apparatus and pancreas.

The x-rays are instructive and of special interest, because they are clear and show excellent mucosal studies by using only small amounts of the contrast material.

The author and his collaborators pay a great deal of attention to gastric and intestinal analysis, stool and various liver and pancreatic tests, plus diet formulas. In America, however, a great deal of work has been done with radioactive isotopes. On the other hand, the authors include tubeless gastric analysis which is of greater importance to the general practitioner. References, bibliography, printing, are well done and the book is recommended highly.

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**CLINICAL RADIOLOGY OF THE SMALL INTESTINES OF ADULTS AND CHILDREN (With the Exception of Acute Conditions). (Radiologie Clinique de L'Intestin Grele de L'Adulte et de L'Enfant—L'occlusion Aigue de L'Adulte Exceptee). P. Porcher, P. Buffard, J. Sauvegrain. Preface by Professor Savy—614 pages, 350 illustrations. Masson and Cie., Paris, 1954.**

The authors first present the general problems which arise from the radiological examination of the small intestine.

The book starts with the explanation of different technics of examination. The technic has to be adapted to any particular case.

After describing the normal radiological anatomy and physiology, the authors give a definition of the elementary reactions of the small intestine, hypo- and hypertony, hypo- and hyperkinesis, variations of the time of transit, troubles of secretion, reabsorption of gas and fluids, and discuss the limitations of the normal and pathological pictures.

A very long chapter is devoted to the child, with many pictures, where one finds,

after a brief embryological survey, all the pathological malformations, which show up sometimes at birth (atresy, ileus meconium, volvulus and malrotation) but which sometimes give only secondary trouble (stenosis, fibrous band). In this chapter we also find the study of invaginations, mesenteric adenitis, Meckel's diverticulum. The chapter ends with a discussion of the evaluation of peristaltic movements in a child.

The study of the adult's small intestine starts with a detailed study of the radiological syndrome of functional insufficiency, with regard to which the authors quote the pathogenic importance of Vitamin B deficiency.

Then, comes a study of different types of sprue, which constitute the major and apparently, primary forms of the functional insufficiency of the small intestine. Studies of allergic intestinal manifestations are discussed which are much more frequent than believed.

Another chapter covers the functional or organo-functional modifications of the small intestine which can be seen in many pathological conditions, without being able to incriminate a Vitamin B deficiency.

Under the title of "small intestine and surgery" an original study is devoted to the aspect of the small intestine after surgical procedures, studying successively, the radiological aspect after resection, the intestinal fistula, modifications of the small intestine after using it as a prothesis in place of the esophagus, the stomach, the bile duct, the ureter, etc. . . . the modifications of the intestine after an operation on the right upper quadrant of the gastrointestinal tract, jejunitis after anastomosis and after gastrectomy, etc. . . .

Excellent roentgenograms are reproduced in the chapter on tumors, all the varieties of benign and malignant, with or without stenosis, are shown. The work ends with a detailed study of pictures of enteritis. A special chapter is devoted to intestinal tuberculosis, in which the interest is centered on an early diagnosis.

The book is written in French, but each chapter has a summary in English and the illustrations have English subtitles. The illustrations are of excellent quality. The print is clear. We can recommend this book most highly to all internists, gastroenterologists, surgeons and roentgenologists.

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**THE DIAGNOSIS OF THE CANCER OF THE STOMACH AT A FAVORABLE STAGE (Le diagnostic du cancer d'estomac a la periode utile): Rene A. Gutmann, Medecin des Hopitaux de Paris. 260 pages, 342 illustrations. G. Doin & Co., Paris, 1956. Price 4,300 fr.**

Dr. Gutmann has just published a new book which deals with the gastric carcinoma at a favorable stage. He has studied this topic for many years and had previously published a book dealing with this condition in 1939. Every gastroenterologist and radiologist has been confronted with the problem of an early recognition of cancer. Any number of cases are seen in which the roentgenological studies, even the most thorough ones, have failed to make the correct diagnosis. It is at this point that this new book fills an important gap. In over 300 roentgenograms, the author shows early cancerous involvement of the stomach, its development, and the differential diagnosis. Not only peptic ulcers, but also antral gastritis, benign fibrosis, hypertrophy of the pylorus and gastritis belong to the conditions, which are occasionally indistiguishable from early carcinoma. It is Gutmann's opinion that cancer of the stomach is much slower in its development than previously expected. Many cases are reproduced, which showed obscure clinical symptoms before a cancerous growth was definitively evident. The roentgenograms of the early periods published in this book will be studied by many who will benefit from this publication. The book is written in French, however, extensive summaries in English are given at the end of each chapter. The reproductions are excellent and instructive. This is a book which can be recommended to all those interested in this field: internists, surgeons, radiologists and gastroenterologists. We congratulate Dr. Gutmann on his new publication.

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1. Straughn, R. A.: Jackson Clin. Bull., 13:83, Aug., 1951.
2. Gray, Horace, and Tainter, M. L.: Am. Jour. Digest. Dis., 8:130, Apr., 1941.

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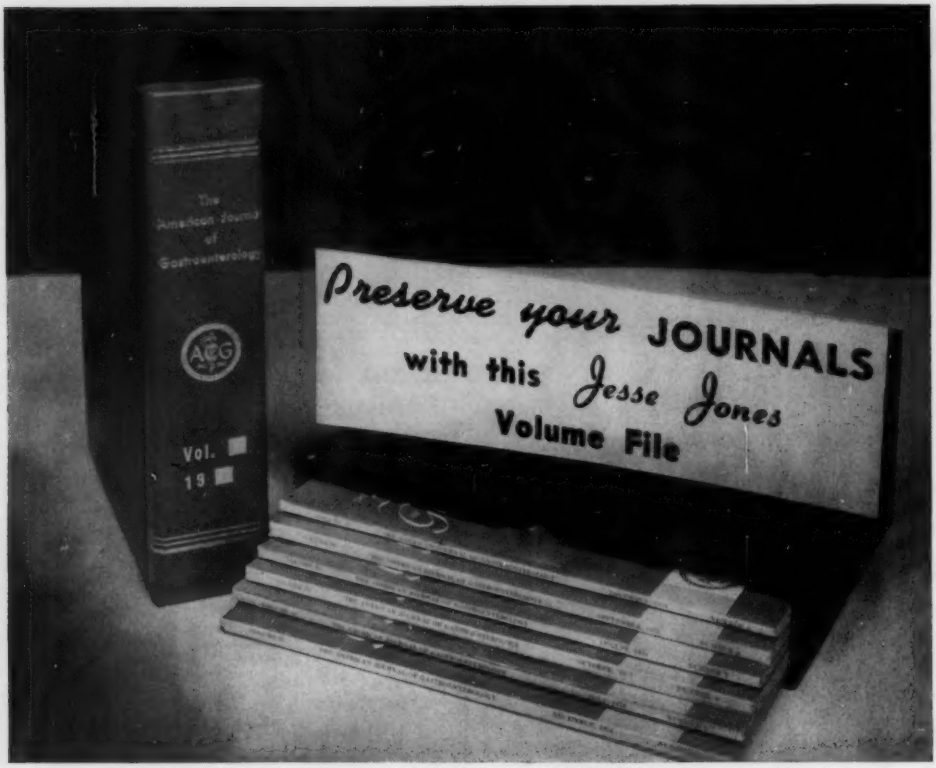


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REFERENCES: 1. Weiss, J.: K.A.G.P. Journal 7:33, 1956. 2. Gabroy, H. K., and Selsman, G. J. V.: Amer. J. Dig. Dis. 20:395, 1953. 3. Lichtman, A. L.: Exper. Med. & Surg. 9:90, 1951.

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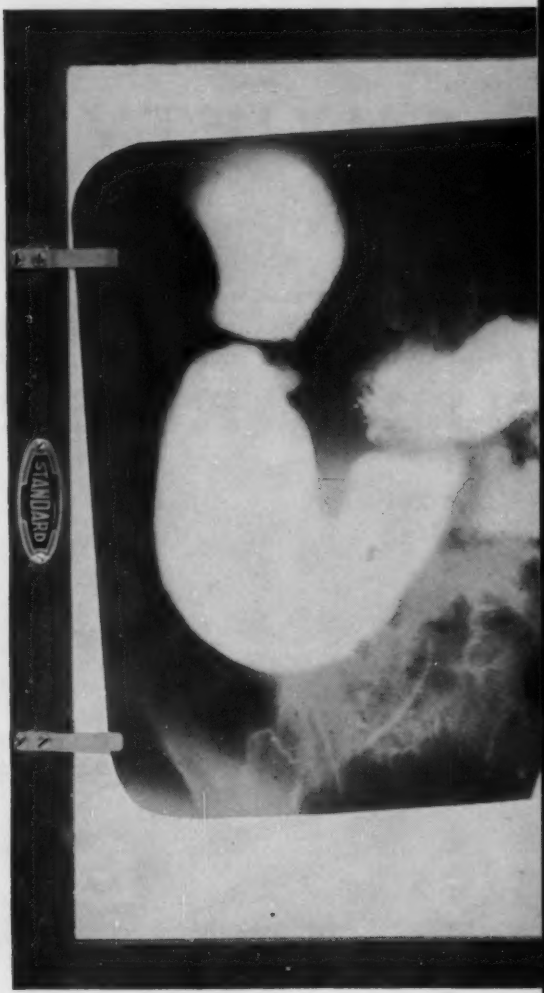


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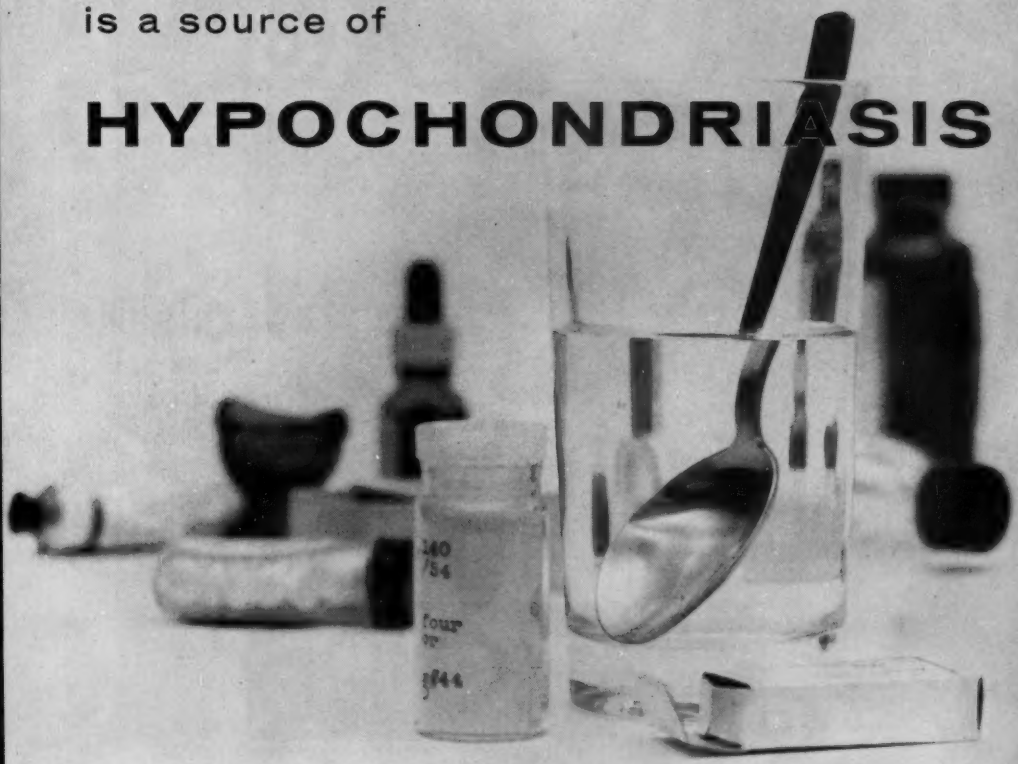

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1. Dolkhart, R. E., Dentler, M. & Barrow, L. L., Ill. M. J. 90:286, 1946.
2. Adler, H. F., Atkinson, A. J., & Ivy, A. C., Am. J. Digest. Dis., 8:197, 1941.
3. Wozasek, D., & Steigman, F., Am. J. Digest. Dis., 9:423, 1942.
4. Williams, R. D., & Olmsted, W. H., Ann. Int. Med., 10:717, 1936.
5. Lieberthal, M. M., Conn. State M. J., 19:86, 1955.

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